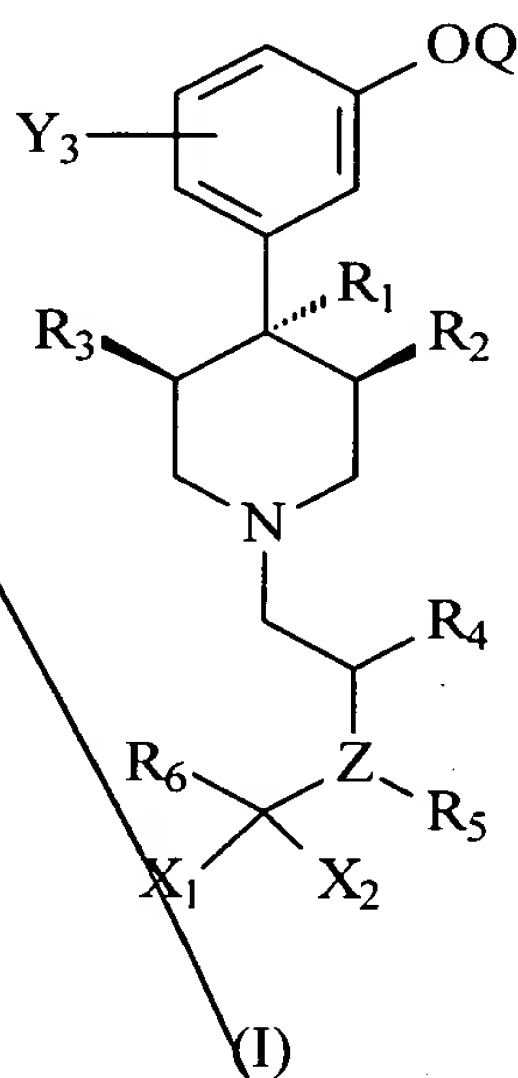


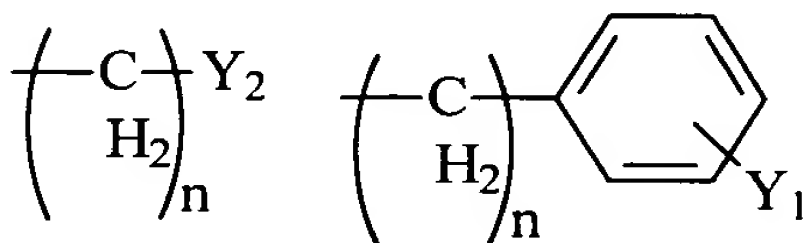
Claims:

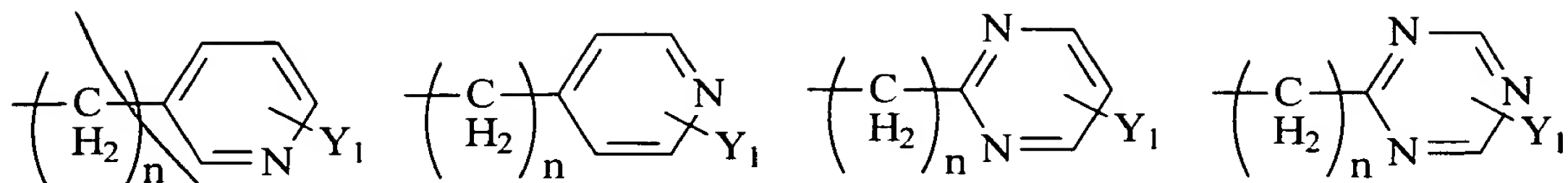
1. A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):



wherein Q is H or COC₁₋₈ alkyl;
R₁ is C₁₋₈ alkyl, or one of the following structures:





Y_1 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $\text{NR}_{10}\text{R}_{11}$, NHCOR_{12} , $\text{NHCO}_2\text{R}_{12}$, $\text{CONR}_{13}\text{R}_{14}$, $\text{CH}_2(\text{CH}_2)_n\text{Y}_2$;

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $\text{NR}_{10}\text{R}_{11}$, NHCOR_{12} , $\text{NHCO}_2\text{R}_{12}$, $\text{CONR}_{13}\text{R}_{14}$, CH_2OH , CH_2OR_8 , COCH_2R_9 ;

Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $\text{NR}_{10}\text{R}_{11}$, NHCOR_{12} , $\text{NHCO}_2\text{R}_{12}$, $\text{CONR}_{13}\text{R}_{14}$, $\text{CH}_2(\text{CH}_2)_n\text{Y}_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1 ;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1 ;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

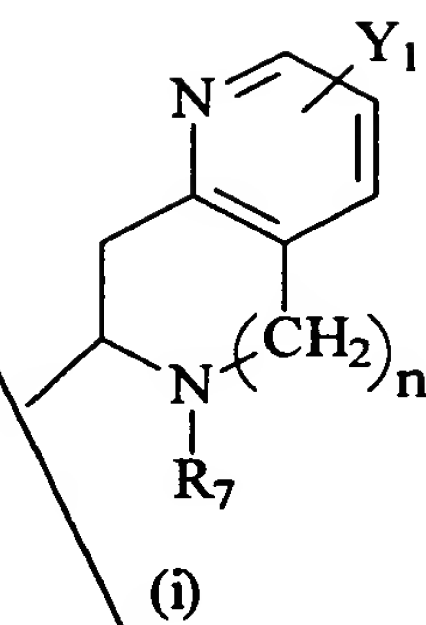
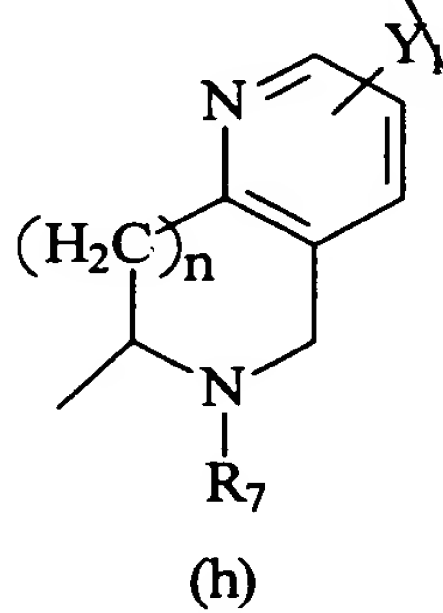
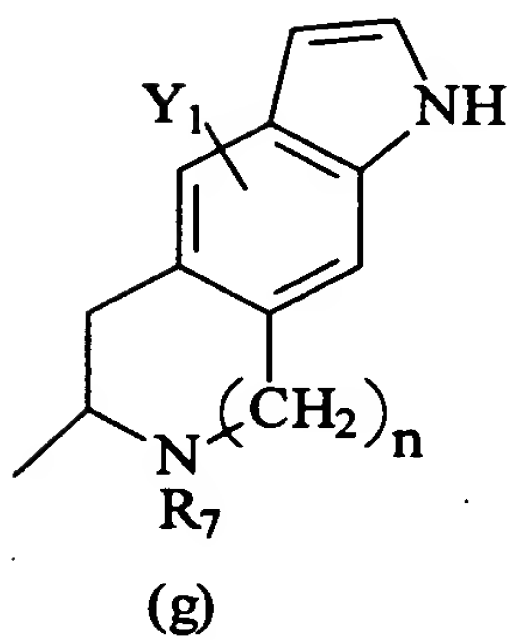
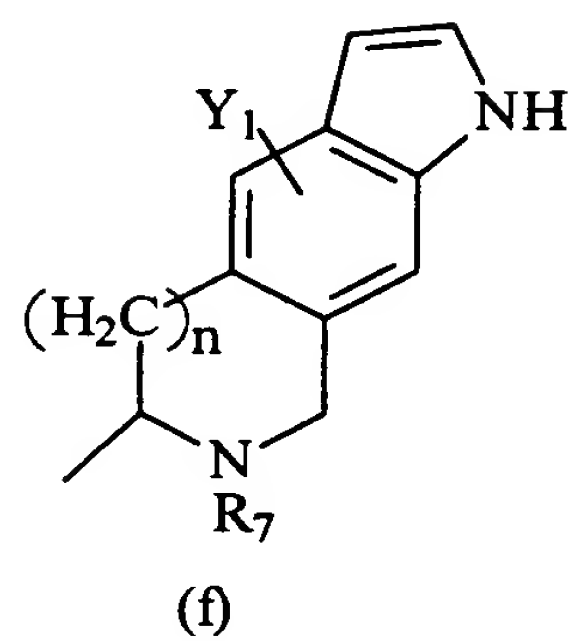
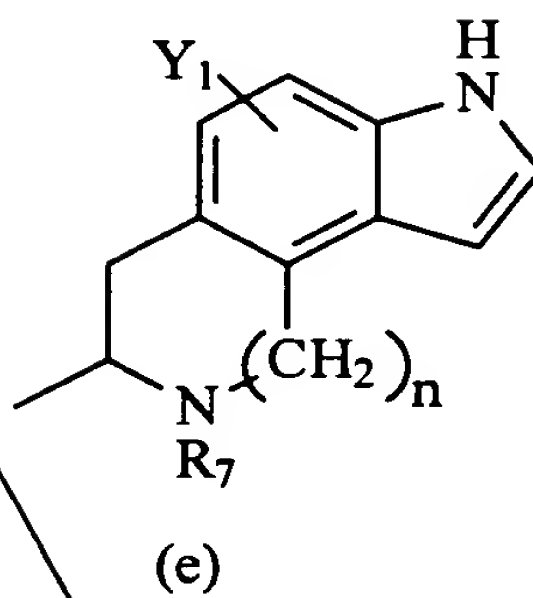
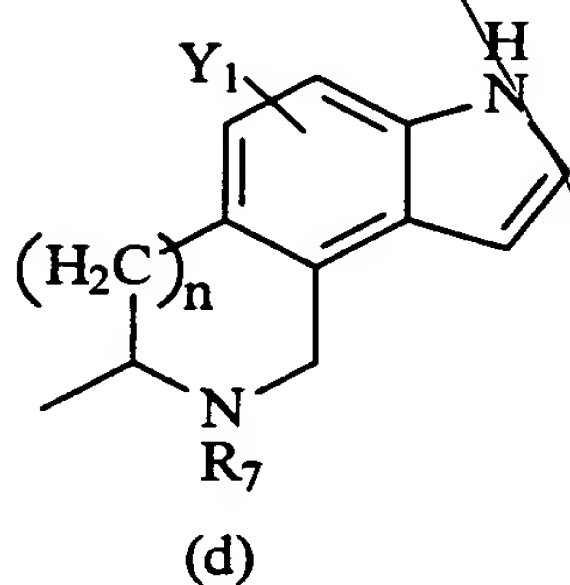
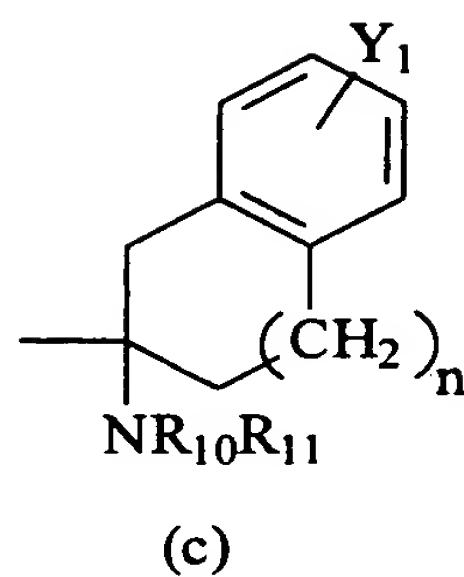
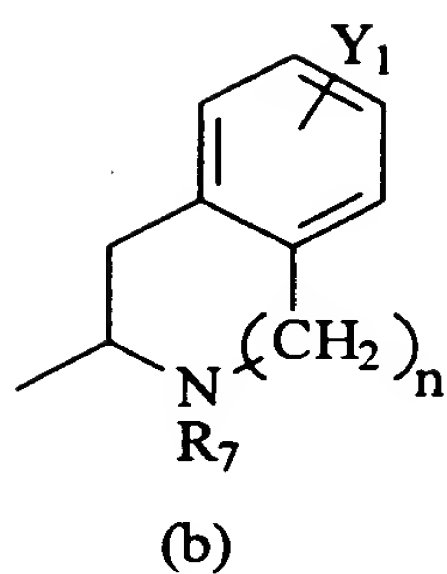
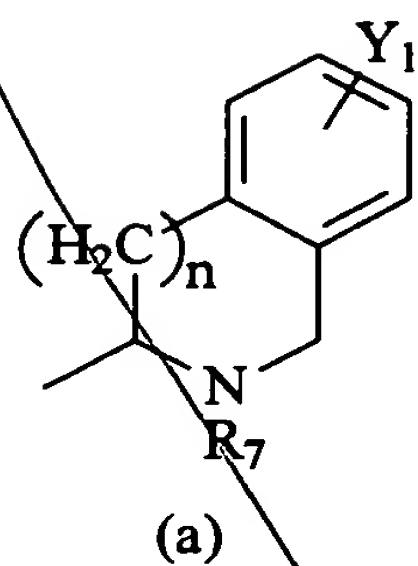
R_4 is hydrogen, C_{1-8} alkyl, $\text{CO}_2\text{C}_{1-8}$ alkylaryl substituted by one or more groups Y_1 , CH_2aryl substituted by one or more groups Y_1 , or $\text{CO}_2\text{C}_{1-8}$ alkyl;

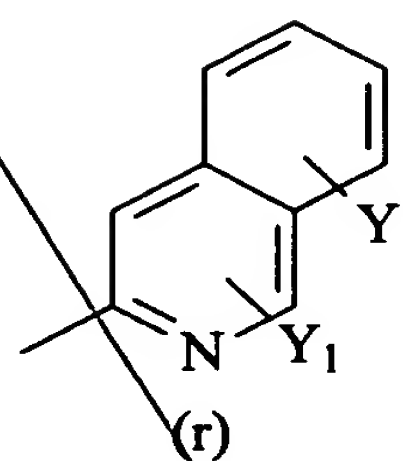
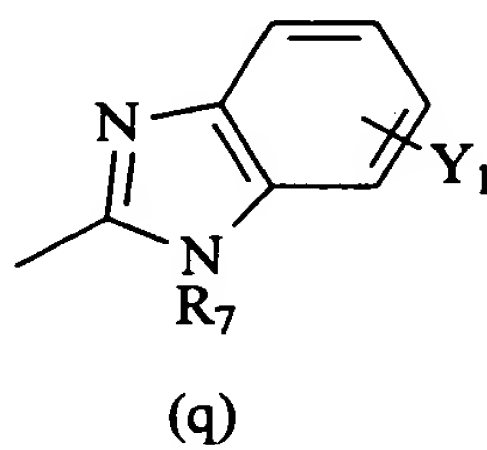
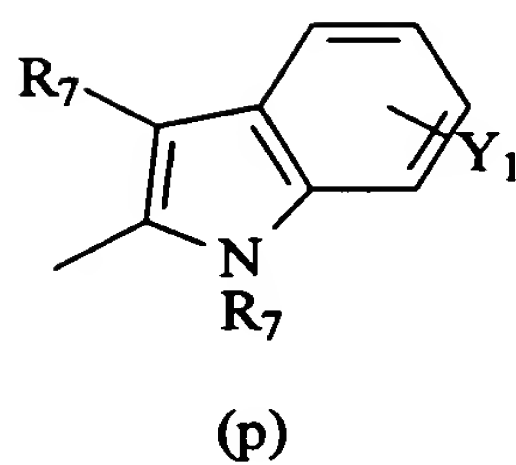
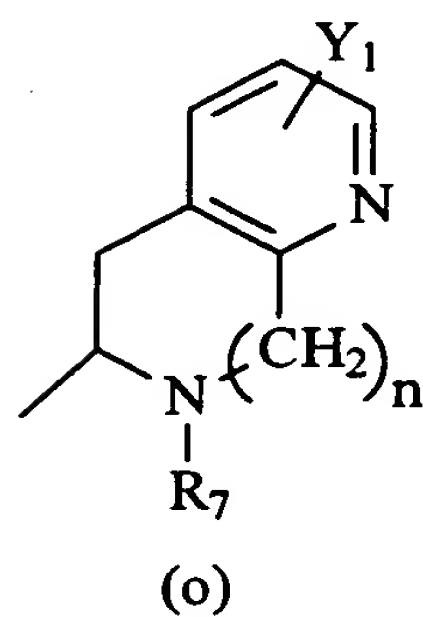
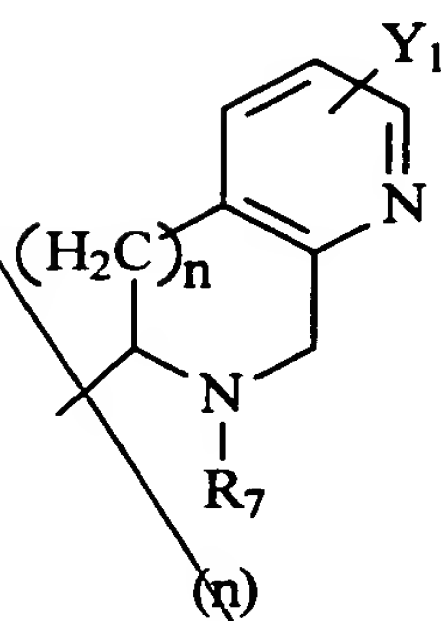
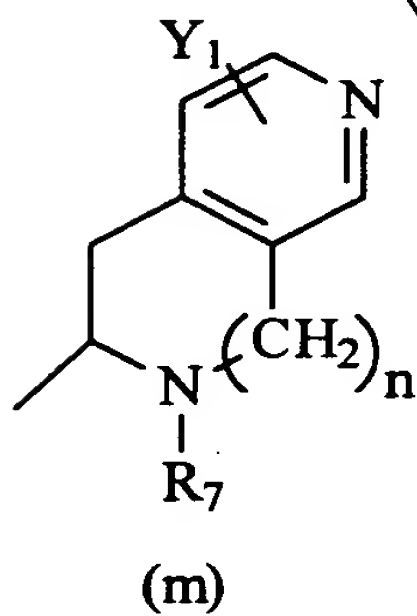
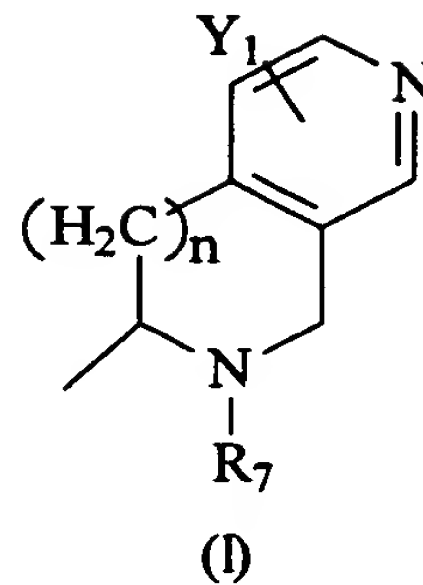
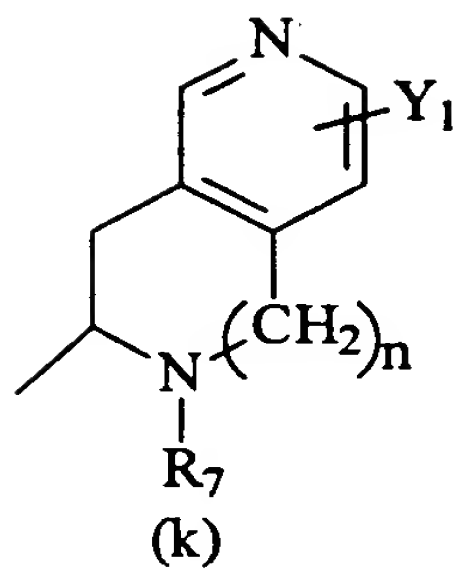
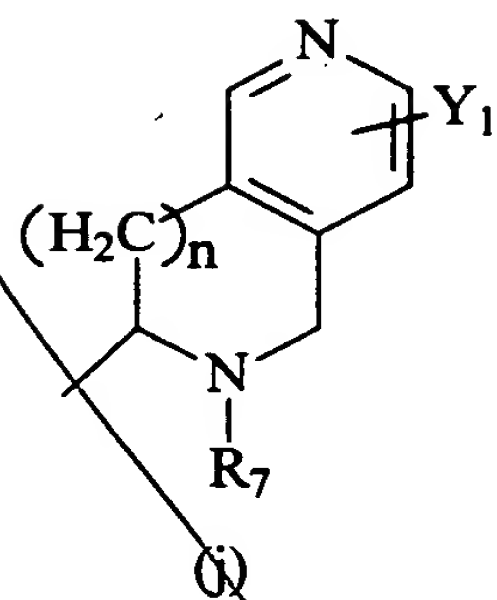
Z is N, O or S; where Z is O or S, there is no R_5

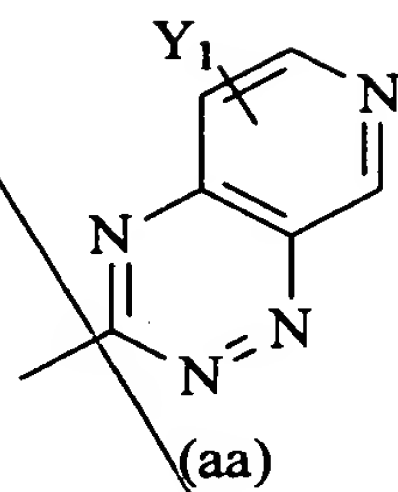
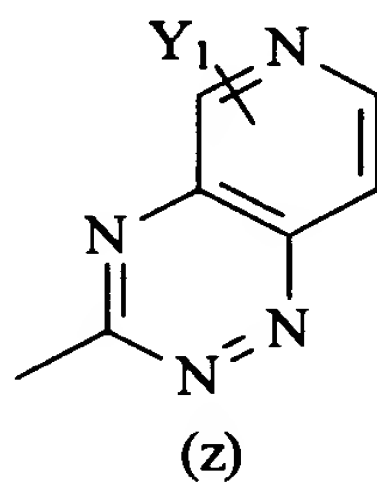
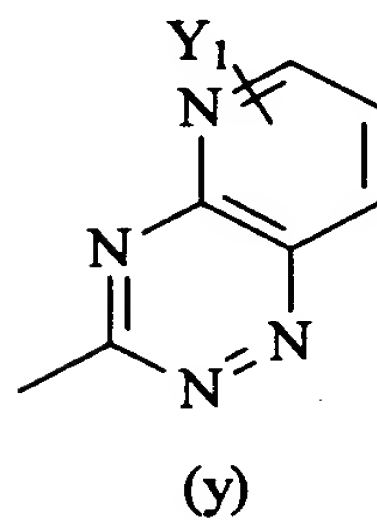
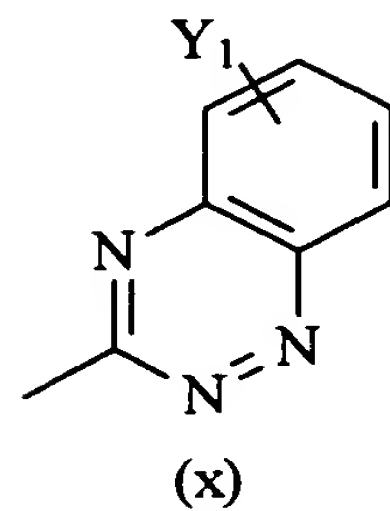
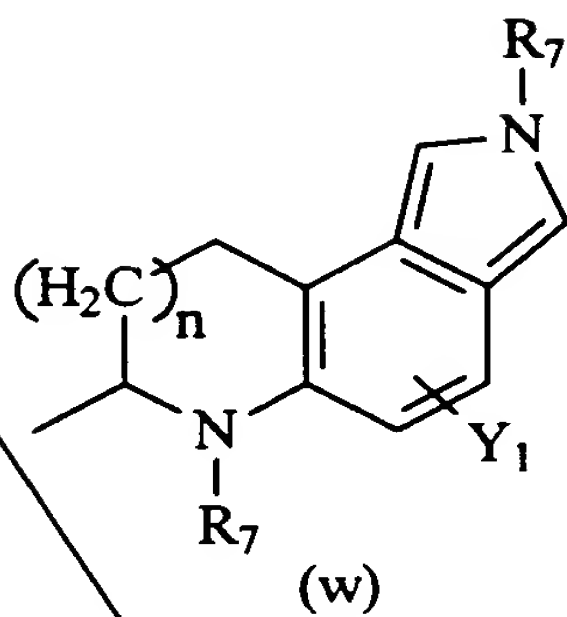
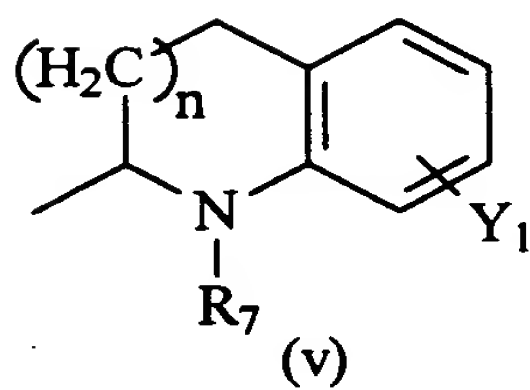
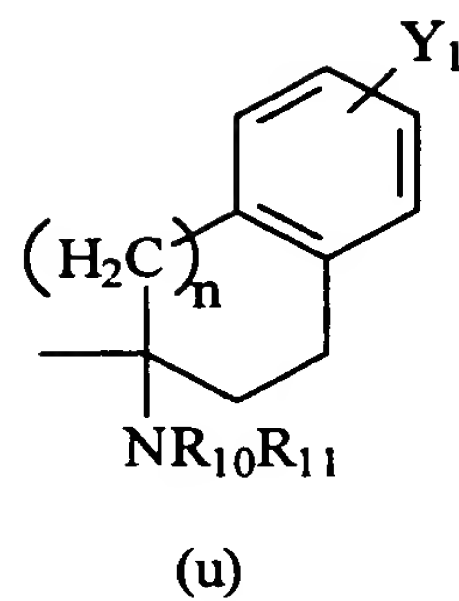
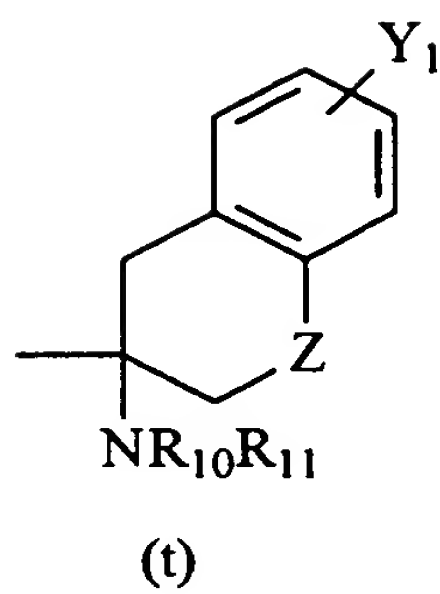
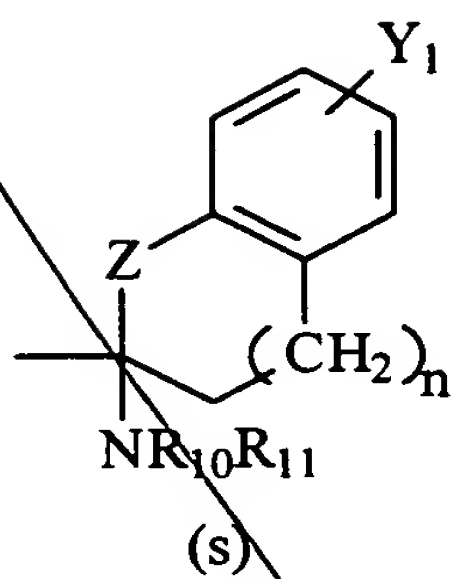
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $\text{CH}_2\text{CO}_2\text{C}_{1-8}$ alkyl, $\text{CO}_2\text{C}_{1-8}$ alkyl or CH_2aryl substituted by one or more groups Y_1 ;

n is 0, 1, 2 or 3;

R_6 is a group selected from the group consisting of structures (a)-(bbb):

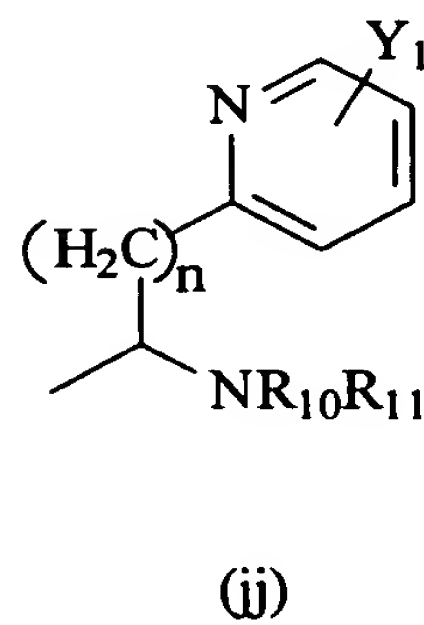
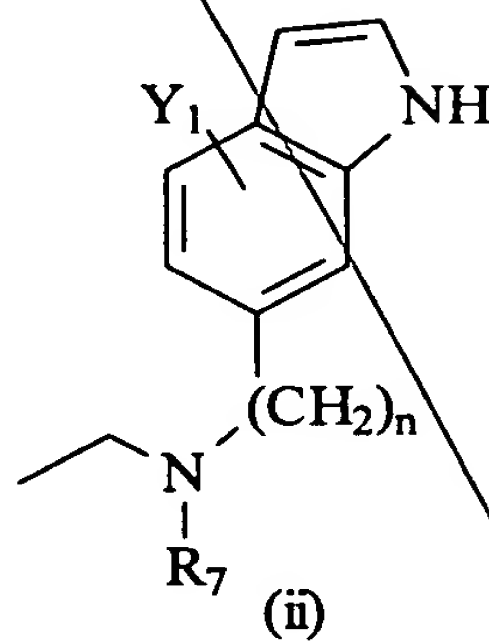
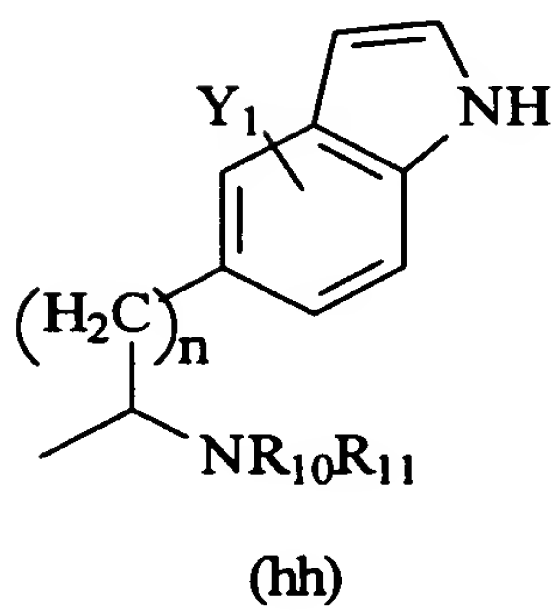
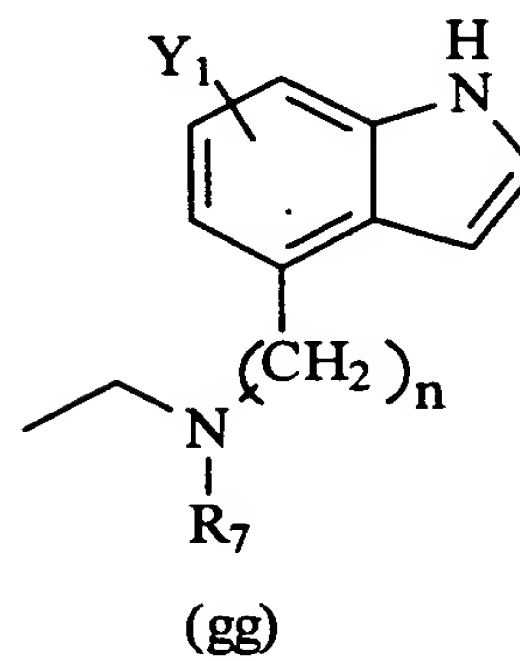
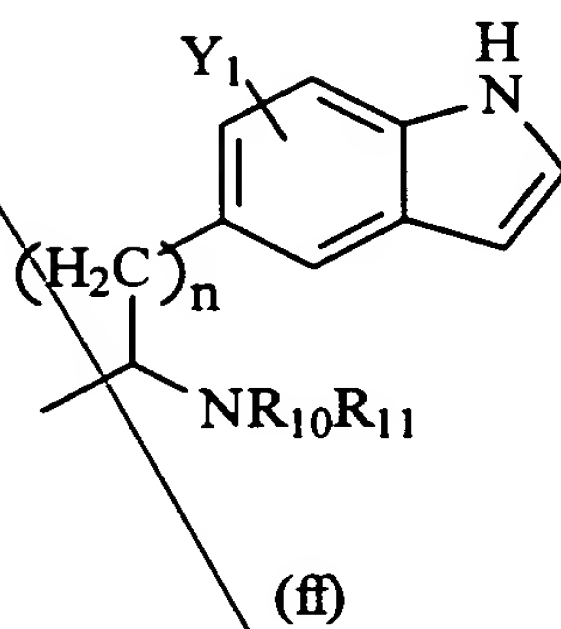
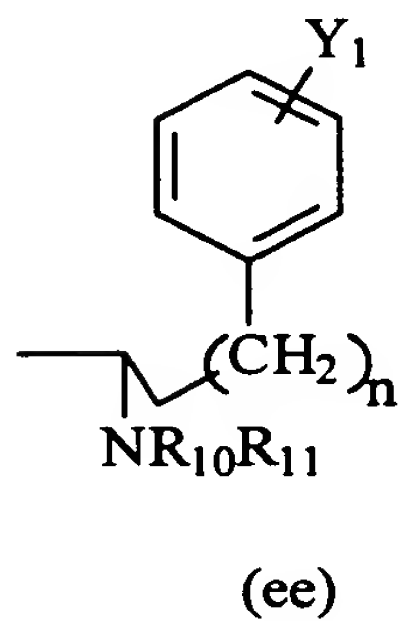
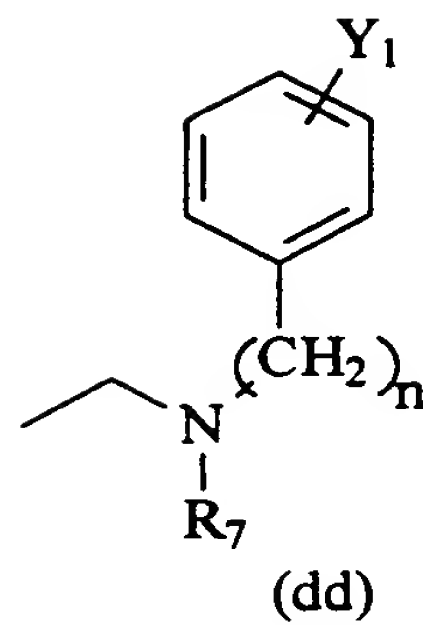
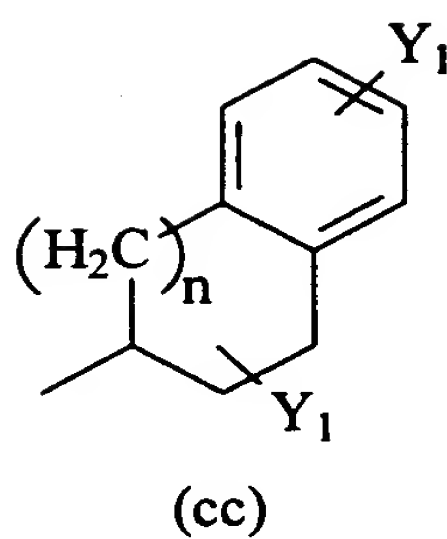
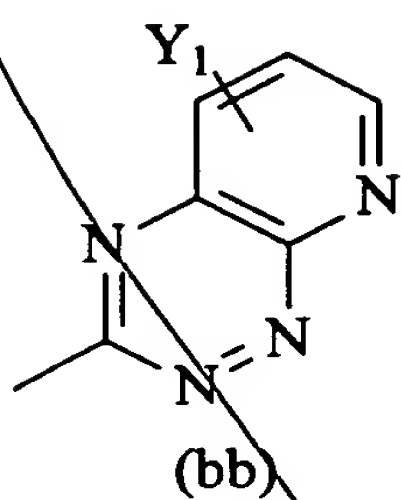


[illegible]

[illegible]

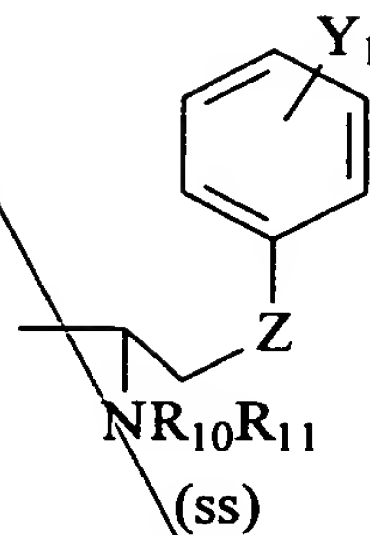
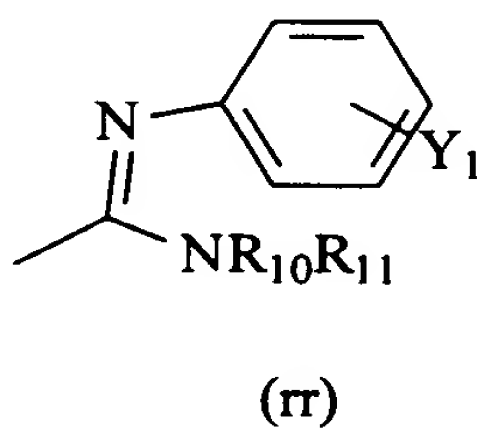
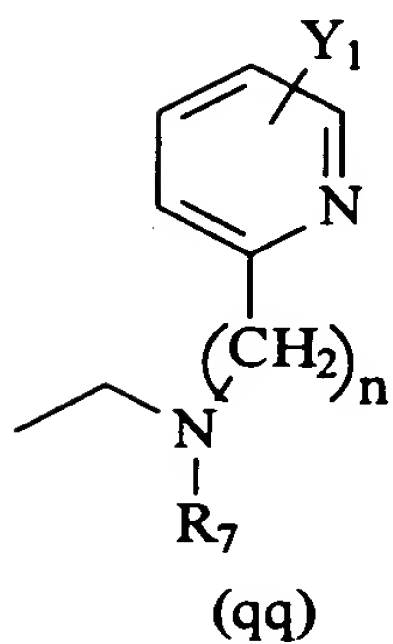
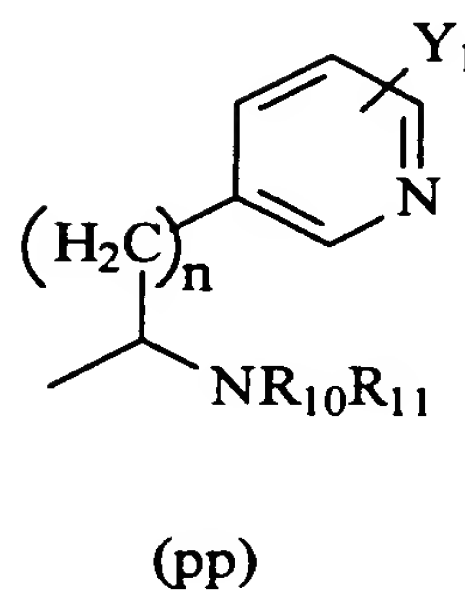
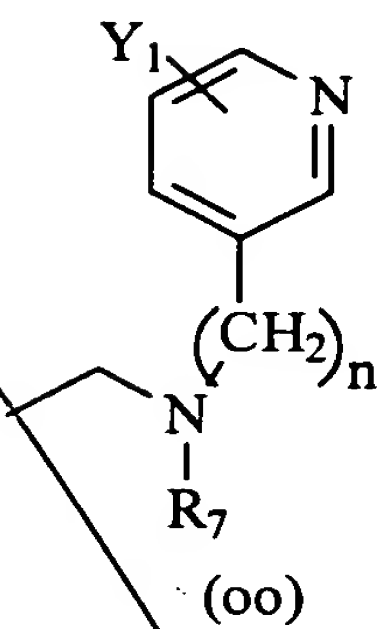
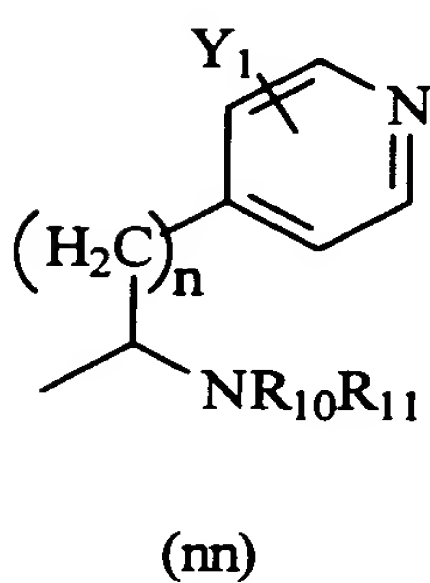
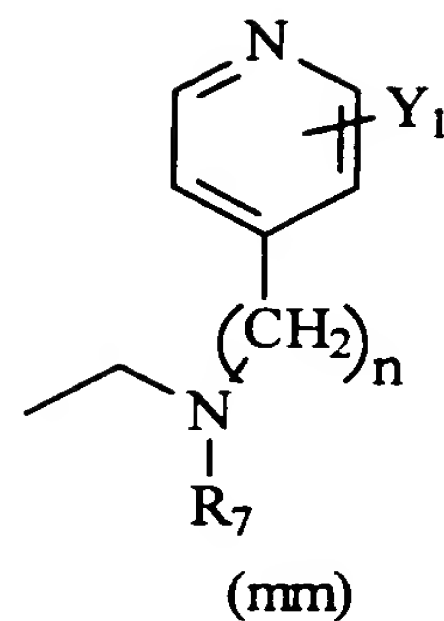
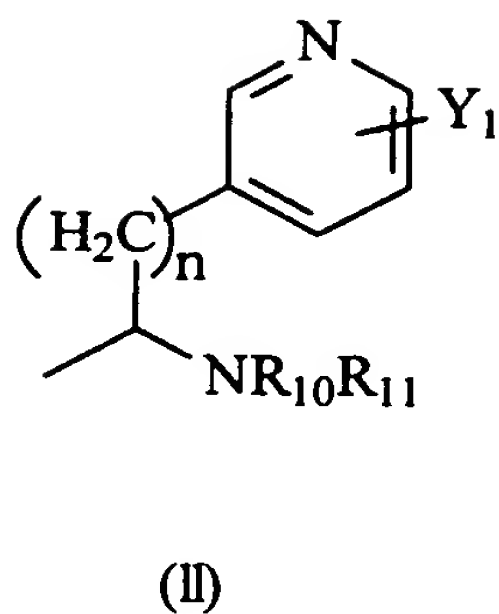
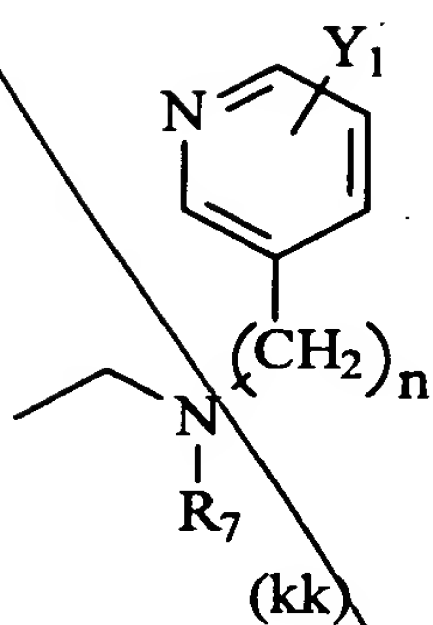
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Chemical structure



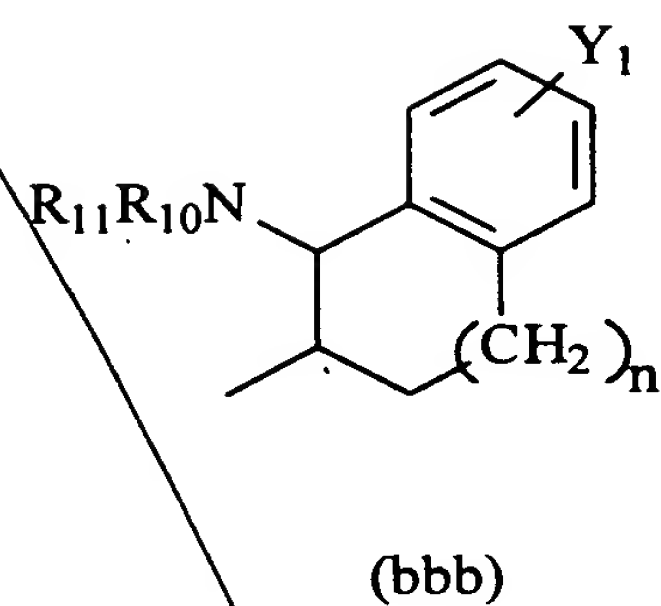
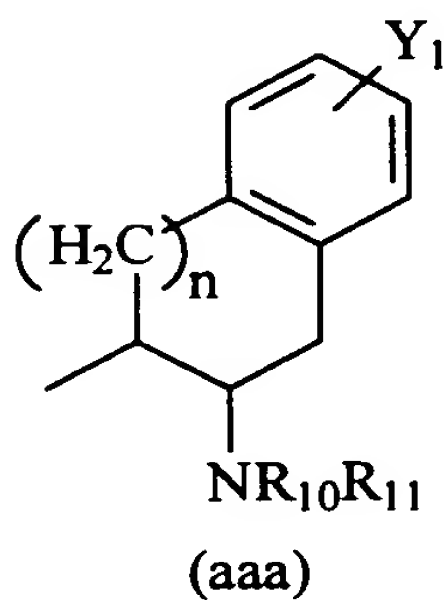
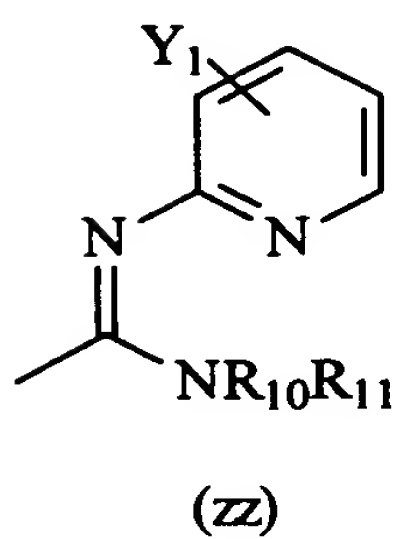
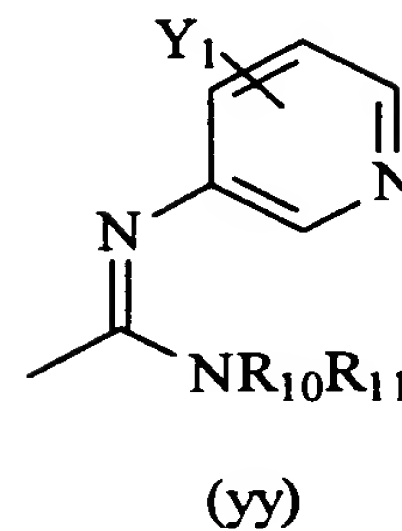
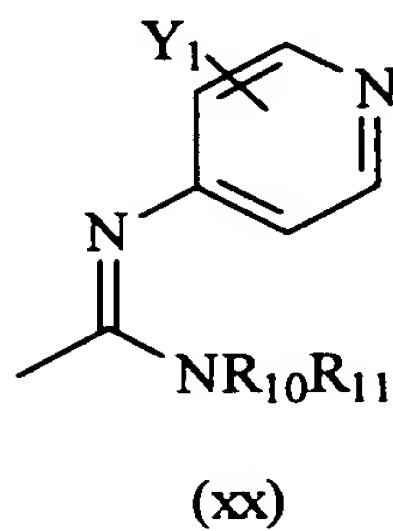
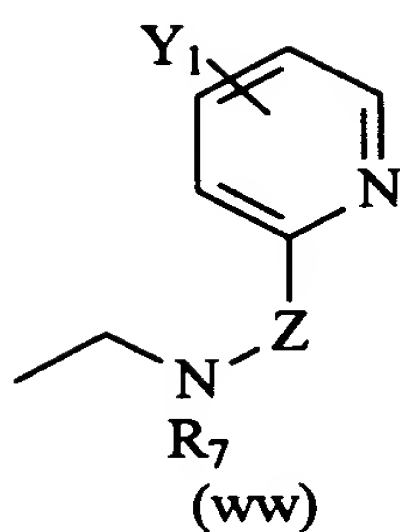
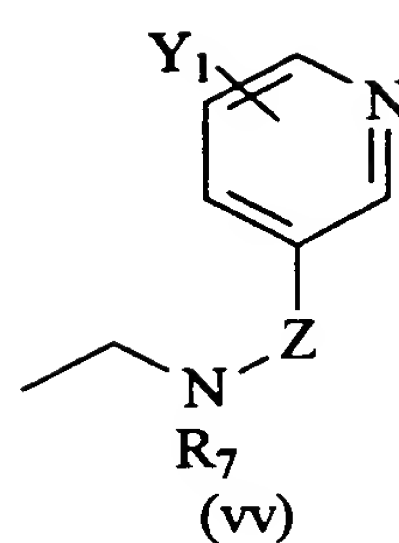
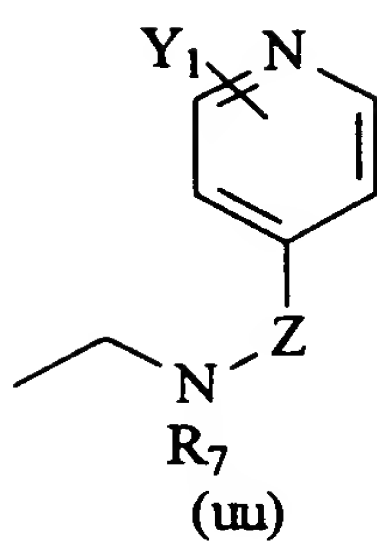
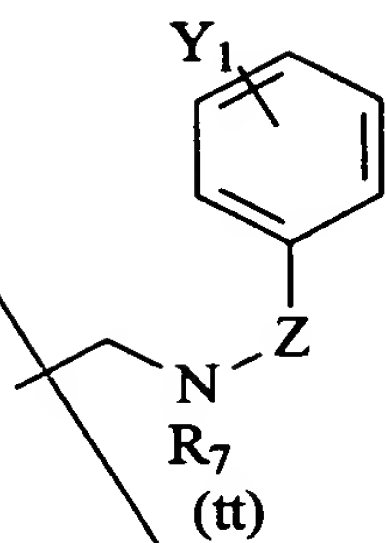
Sub
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Chemical Abstracts



Sub
158

Chemical



X₁ is hydrogen, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl;

X₂ is hydrogen, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl;

or X₁ and X₂ together form =O, =S, =NH;

R₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,

5 NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, CH₂(CH₂)_nY₂, C(=NH)NR₁₆R₁₇;

R₈ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CONR₁₃R₁₄,
CH₂(CH₂)_nY₂;

R₉ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₀ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₁ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₂ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₃ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₄ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₅ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₆ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

and

R₁₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂.

2. The method of claim 1, wherein said kappa opioid receptor antagonist is a
compound of formula (I), wherein R₁, R₄, R₅, Y₁, Y₂, Z, n, X₁, X₂, and R₇-R₁₇ are as indicated
above;

Y₃ is H;

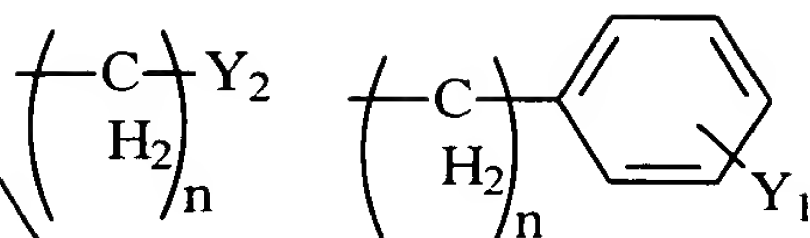
R₂ and R₃ are each, independently, H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, CH₂ aryl
substituted by one or more substituents Y₁; and

R₆ is a group having a formula selected from the group consisting of structures (a)-
(cc).

and pharmaceutically acceptable salts thereof.

3. The method of claim 1, wherein said kappa opioid receptor antagonist is a
compound of formula (I) wherein Y₁, Y₂, R₄, R₅, Z, n, X₁, X₂ and R₈-R₁₅ are as indicated
above;

R₁ is C₁₋₈ alkyl,



Y₃ is H;

R₂ and R₃ are each, independently, H or C₁₋₈ alkyl, wherein R₂ and R₃ cannot both be H at the same time;

R₆ is a formula selected from the structures (a)-(r); and

R₇ is H, C₁₋₈ alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

4. The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₅ are as noted above;

R₁ is C₁₋₈ alkyl;

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, COCH₂R₉;

Y₃ is H;

R₂ and R₃ are each, independently, H or methyl, wherein R₂ and R₃ cannot both be H at the same time;

15 R₄ is H, C₁₋₈ alkyl, CO₂C₁₋₈alkyl, aryl substituted by one or more substituents Y₁ and the stereocenter adjacent to R₄ is in an (S) configuration;

R₅ is H, C₁₋₈ alkyl, CH₂CO₂C₁₋₈ alkyl;

R₆ is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

20 R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

5. The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₄ are as indicated above;

R_1 is methyl,

Y_2 is H, CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$,
 CH_2OH , CH_2OR_8 , $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

R_4 is C_{1-8} alkyl, CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration
of (S);

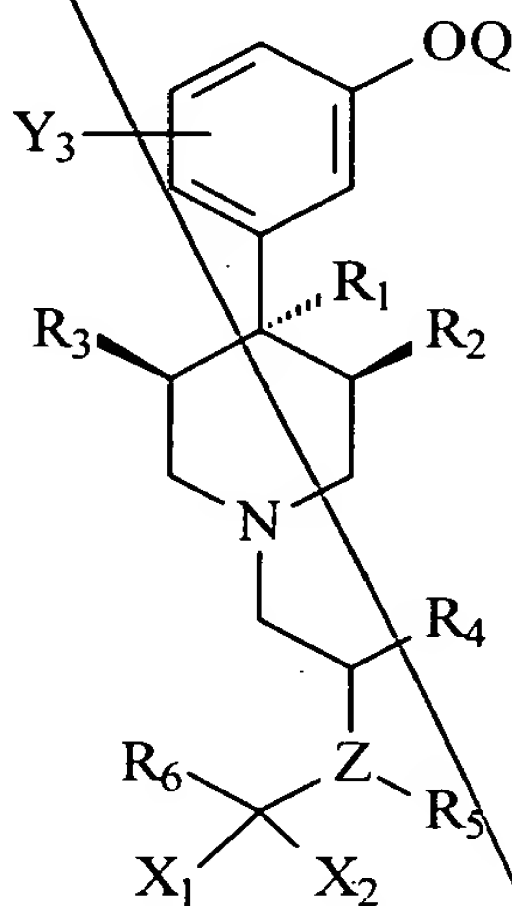
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and
(b); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or
 $CH_2(CH_2)_nY_2$.

6. The method of claim 1, wherein said kappa opioid receptor antagonist is a
compound selected from formulae 14-21 of Fig. 1.

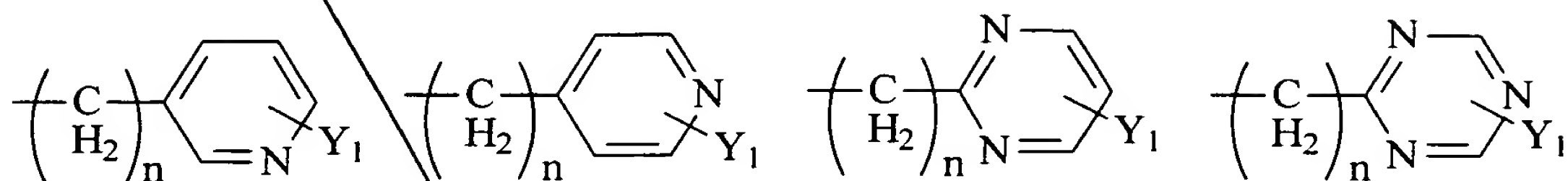
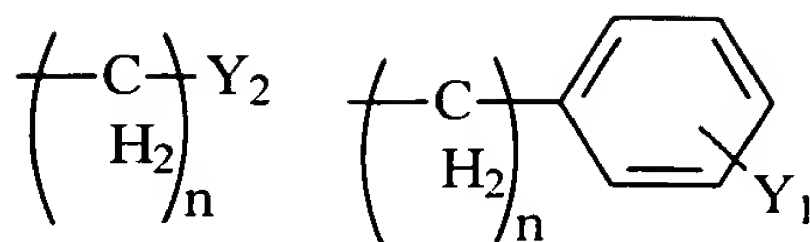
7. A kappa opioid receptor antagonist compound represented by the formula (I):



(I)

wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y₁ is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂(CH₂)_nY₂;

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, COCH₂R₉;

Y₃ is H, OH, Br, Cl, F, CN, CF₃, NO₂, N₃, OR₈, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂(CH₂)_nY₂;

R₂ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl or CH₂aryl substituted by one or more groups Y₁;

R₃ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl or CH₂aryl substituted by one or more groups Y₁;

wherein R₂ and R₃ may be bonded together to form a C₂₋₈ alkyl group;

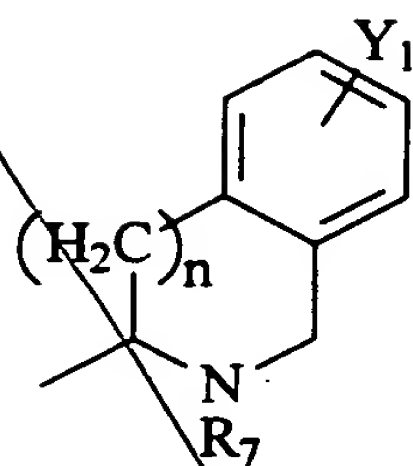
R₄ is hydrogen, C₁₋₈ alkyl, CO₂C₁₋₈ alkylaryl substituted by one or more groups Y₁, CH₂aryl substituted by one or more groups Y₁ or CO₂C₁₋₈ alkyl;

Z is N, O or S; when Z is O or S there is no R₅;

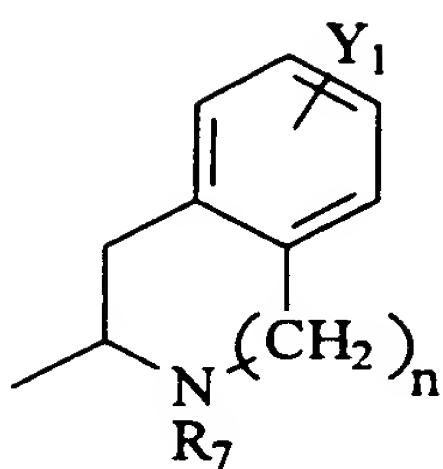
R₅ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, CH₂CO₂C₁₋₈ alkyl, CO₂C₁₋₈ alkyl or CH₂aryl substituted by one or more groups Y₁;

n is 0, 1, 2 or 3;

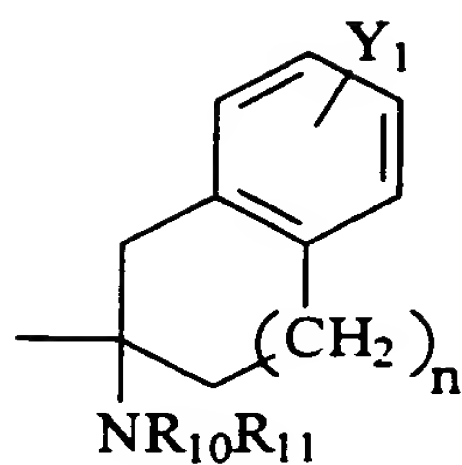
R₆ is a group selected from the group consisting of structures (a)-(bbb):

[illegible]

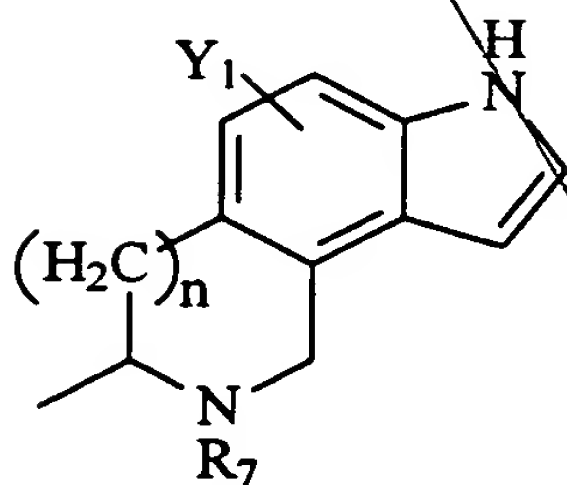
(a)



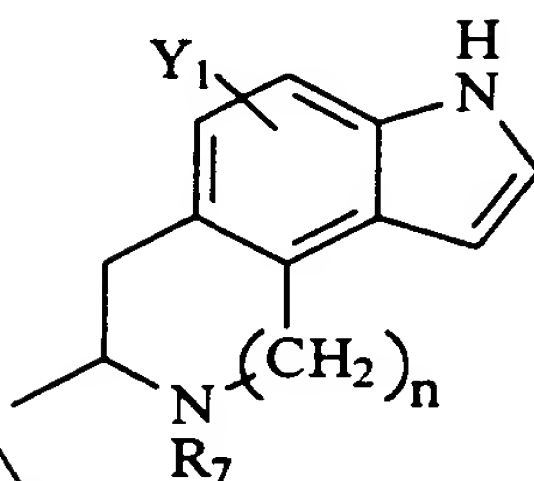
(b)



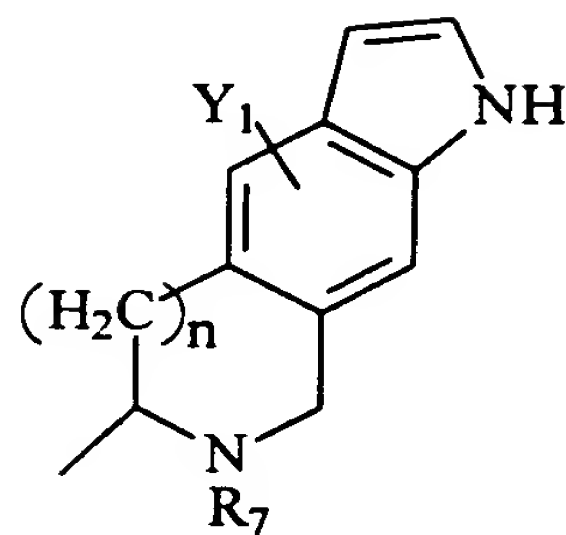
(c)



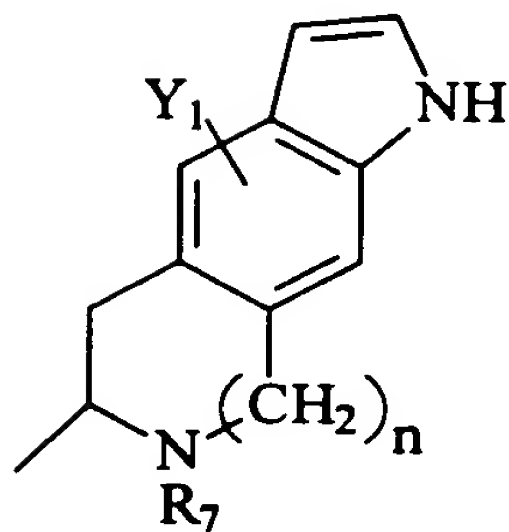
(d)



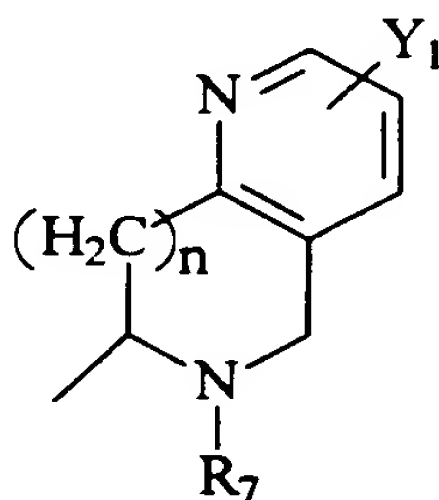
(e)



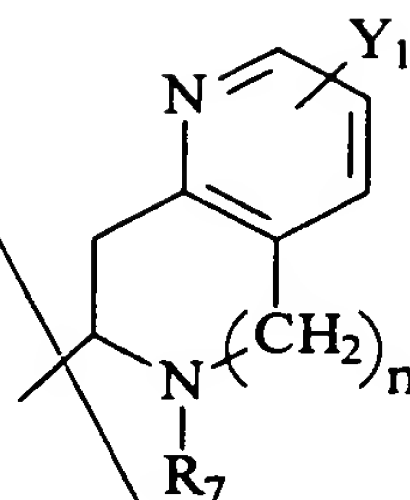
(f)



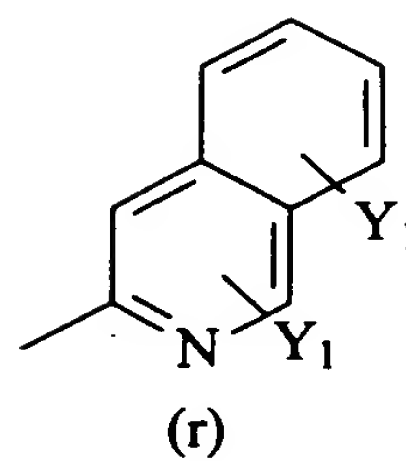
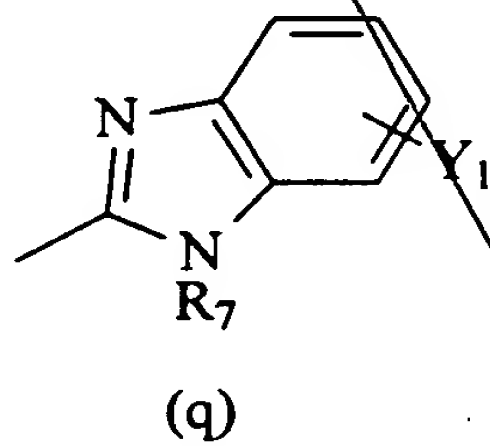
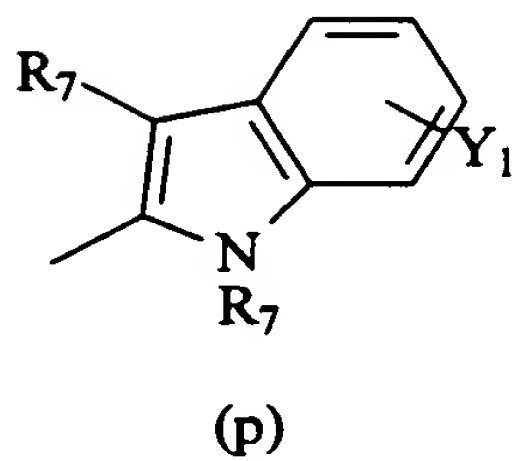
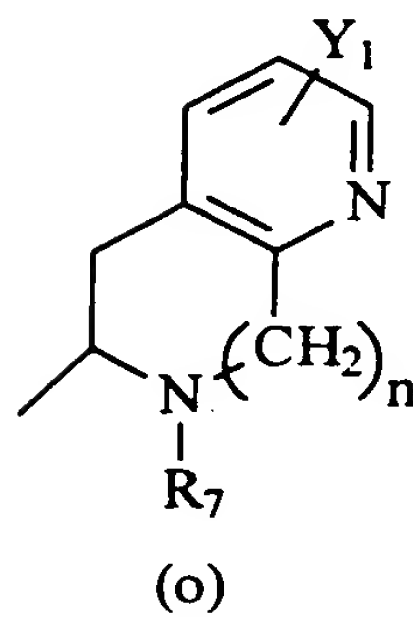
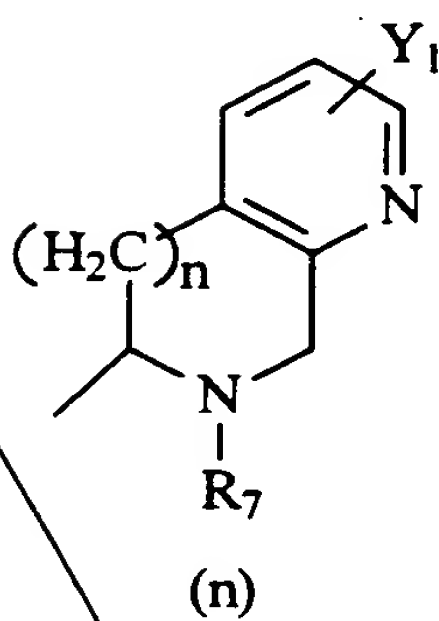
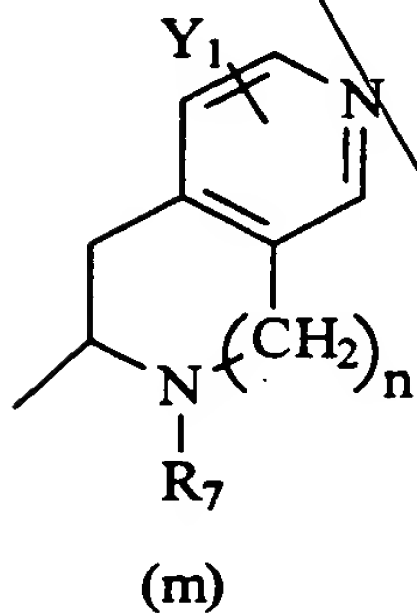
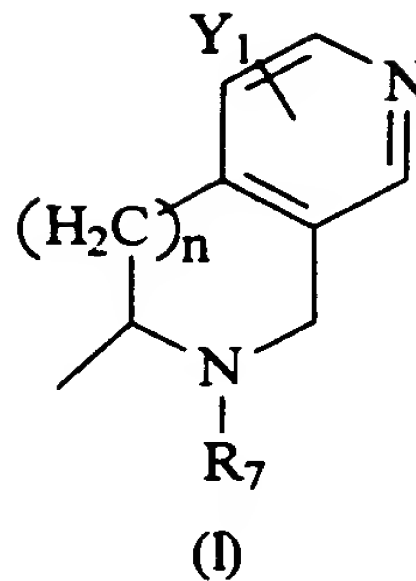
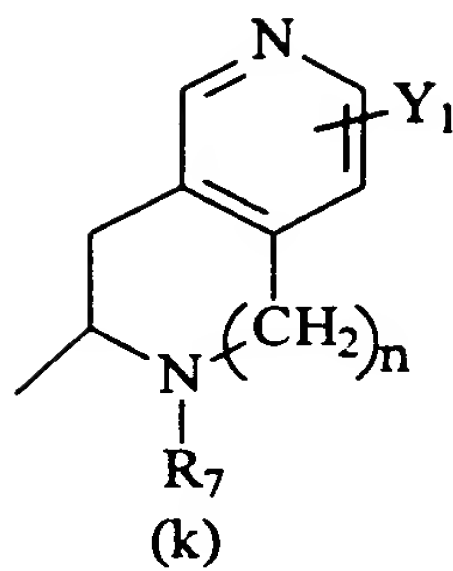
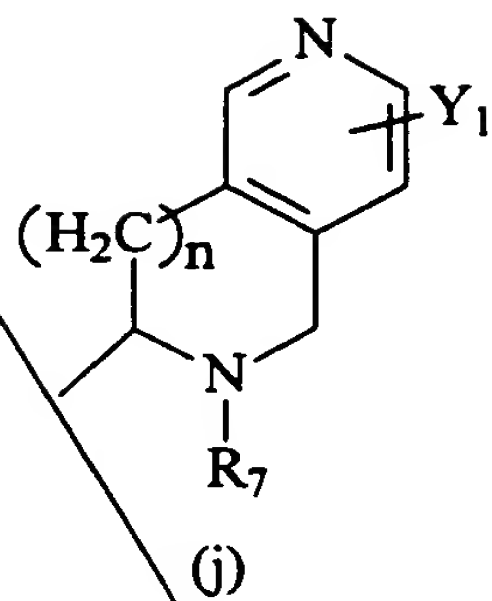
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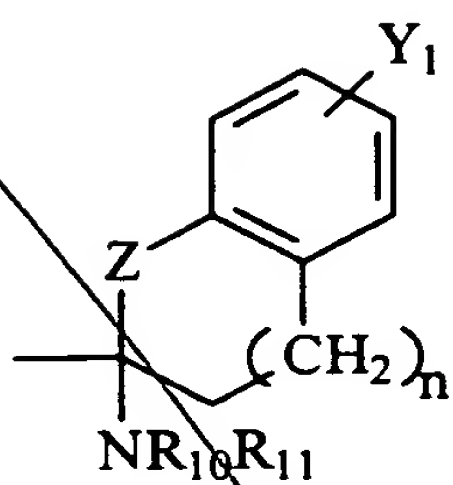


(h)

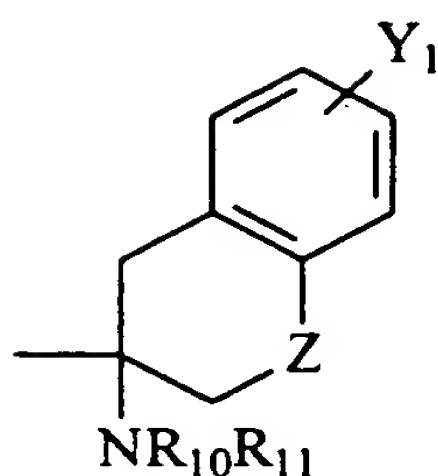


(1)

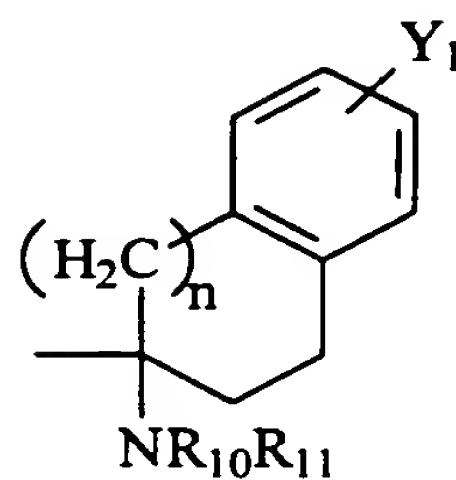
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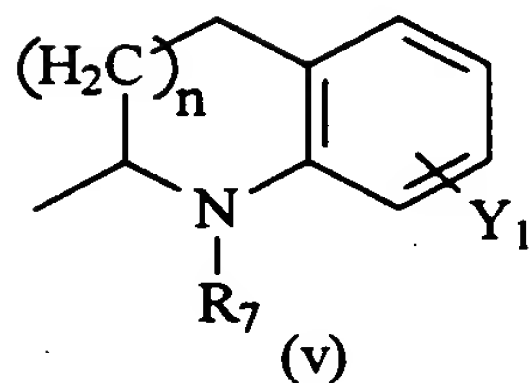
(s)



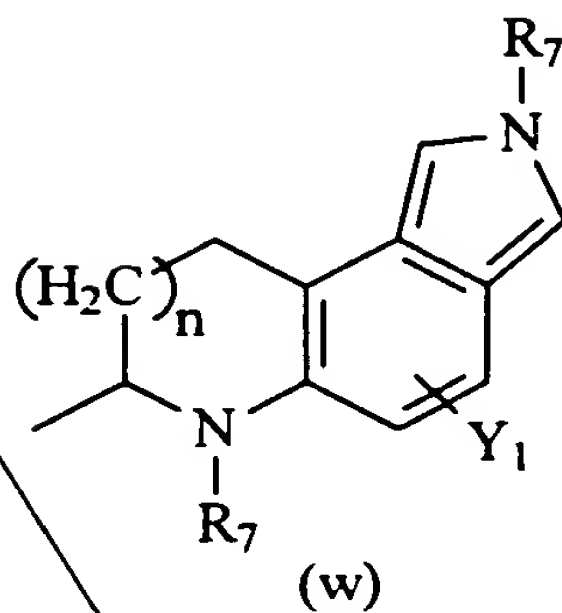
(t)



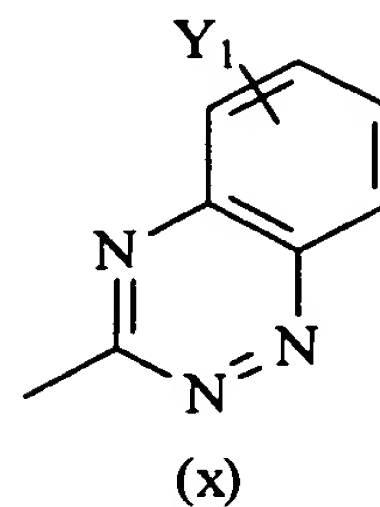
(u)



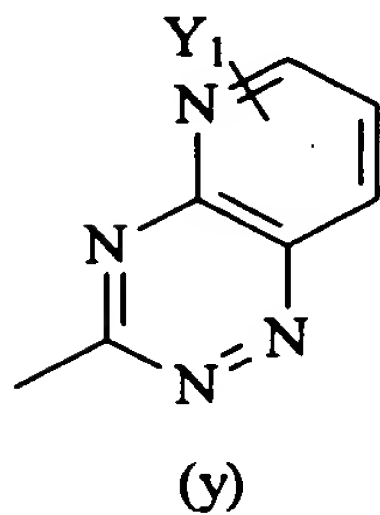
(v)



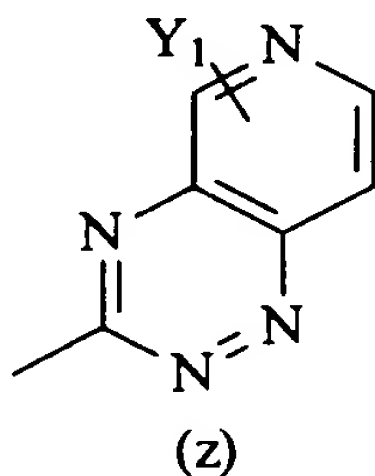
(w)



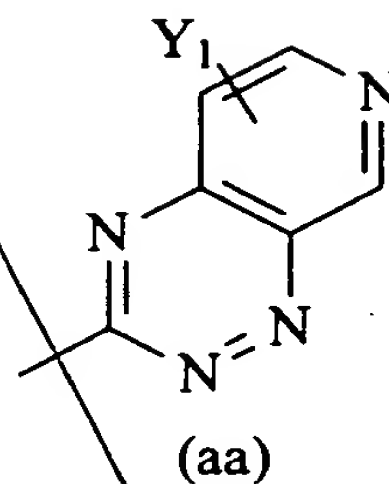
(x)



(y)

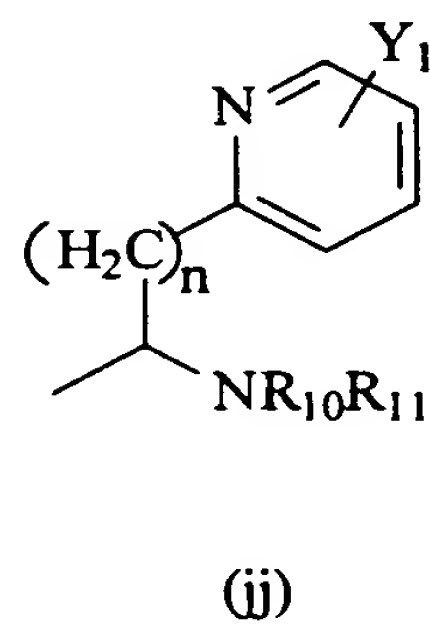
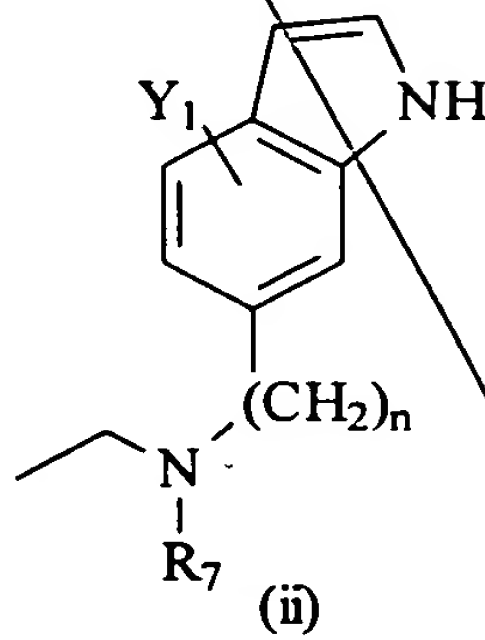
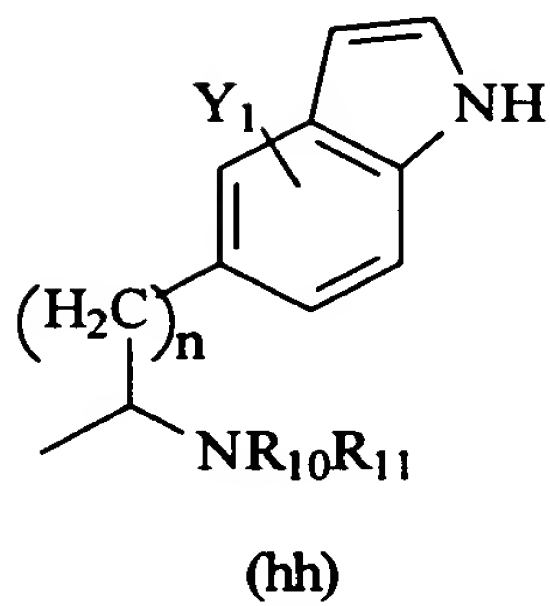
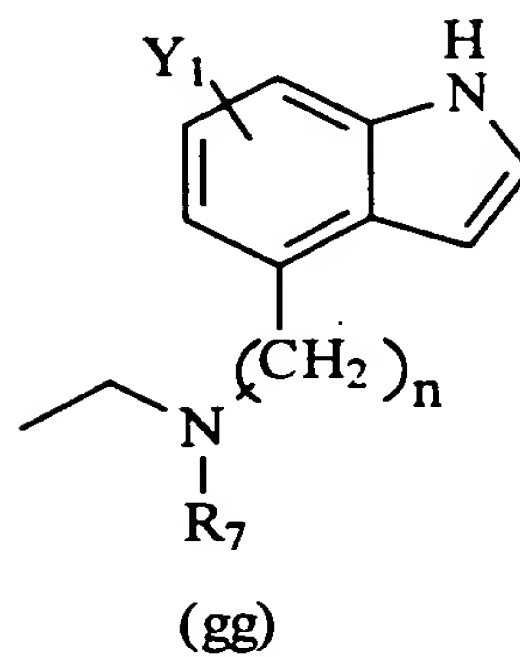
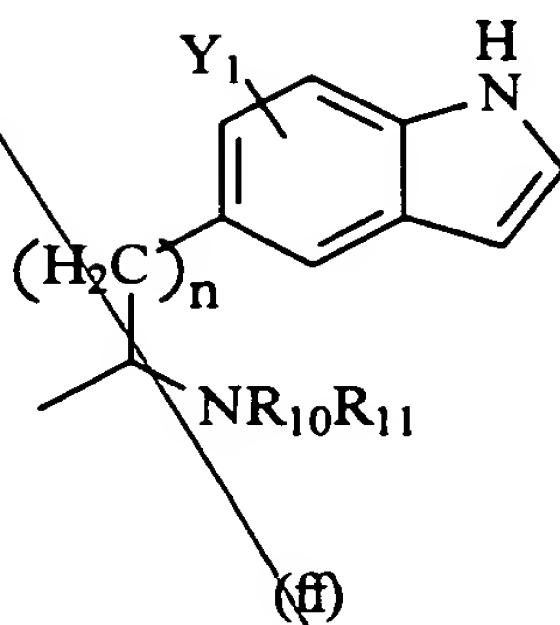
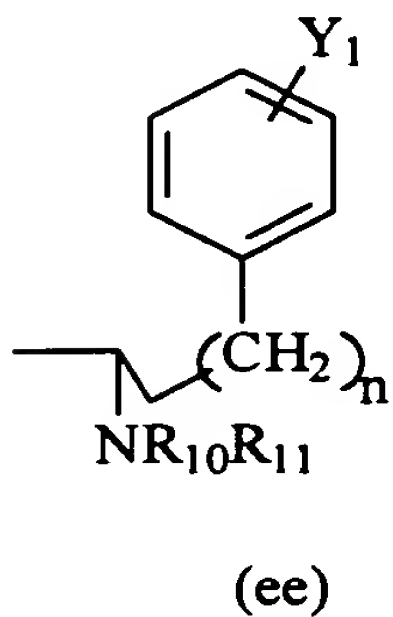
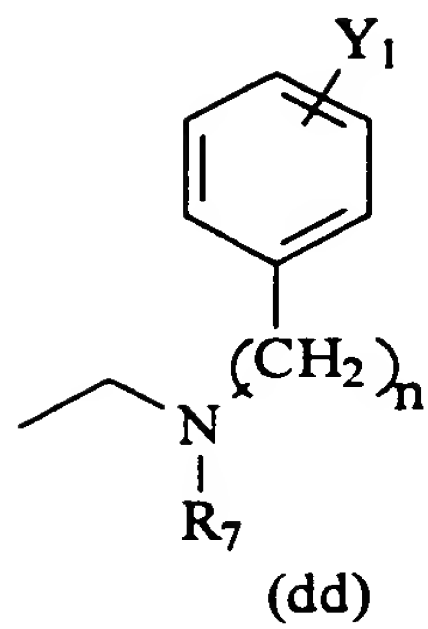
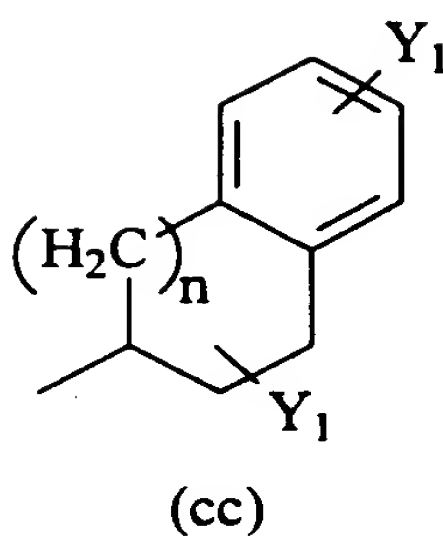
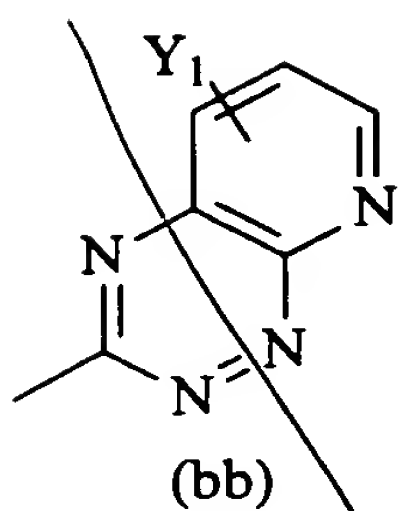


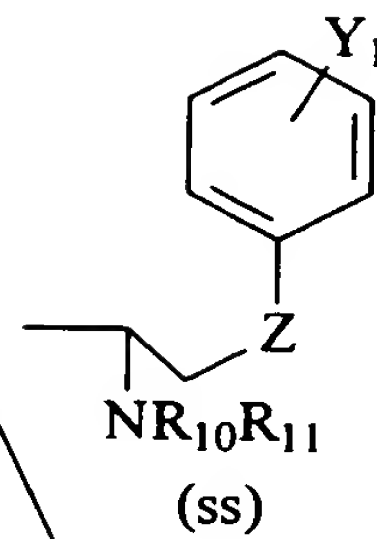
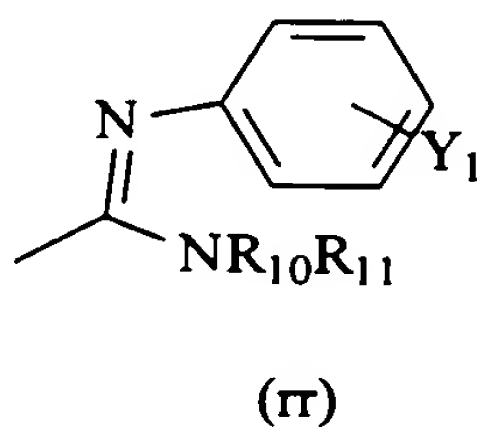
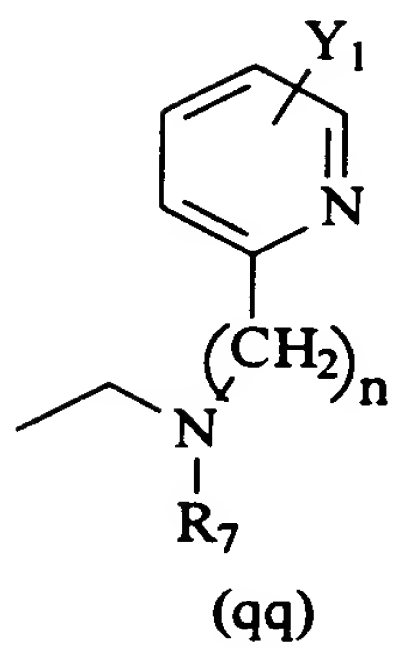
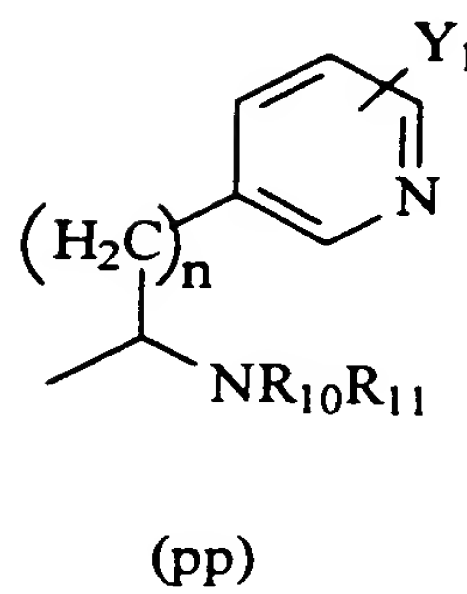
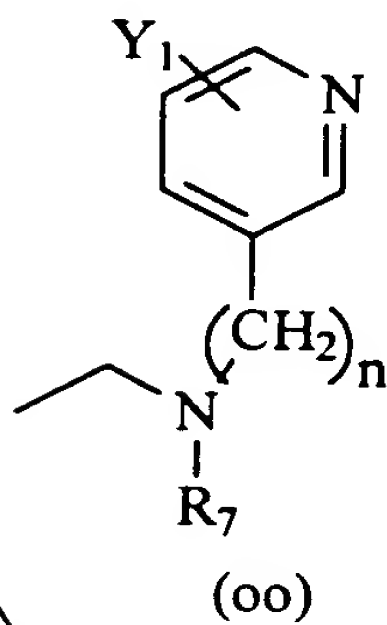
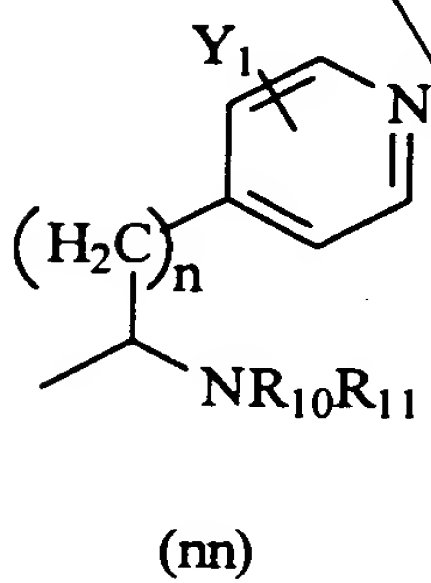
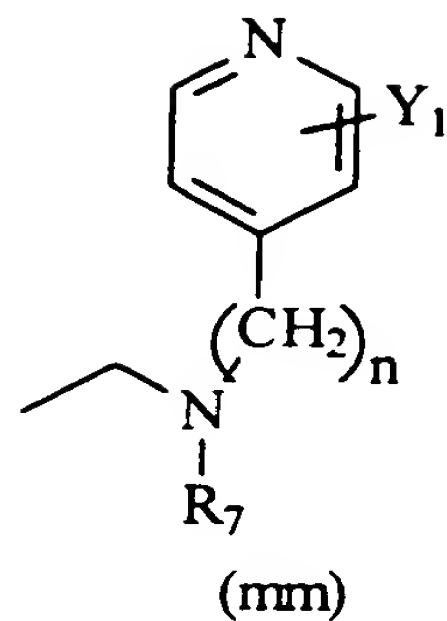
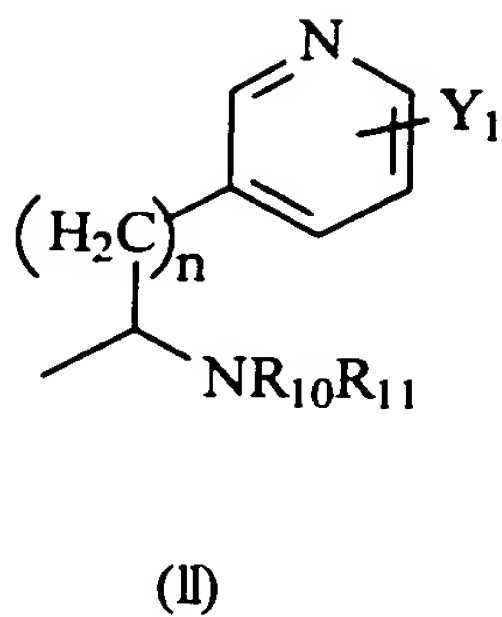
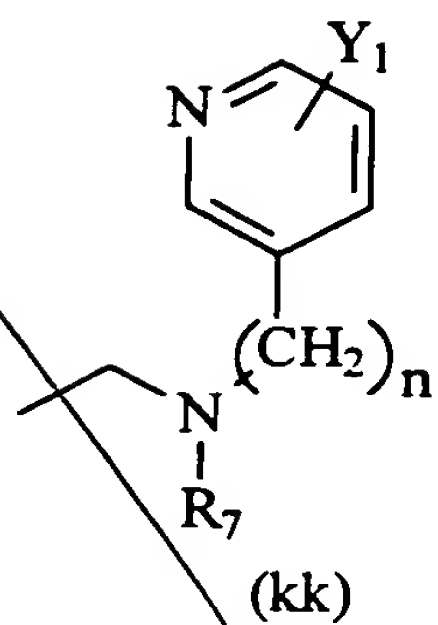
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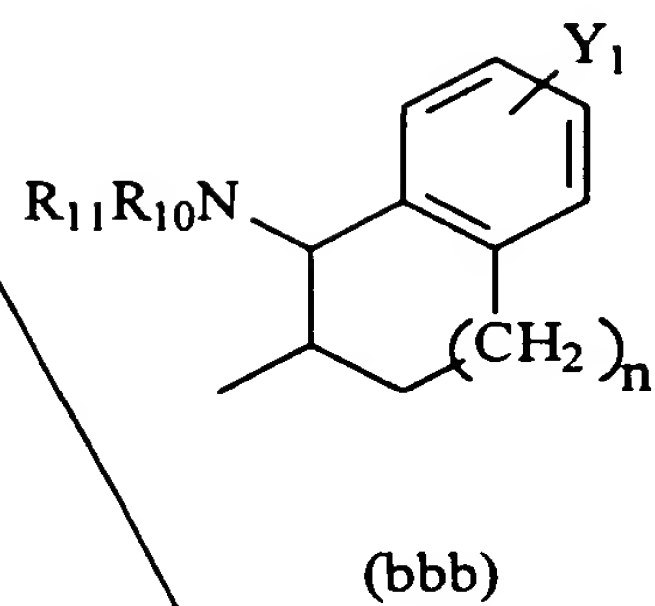
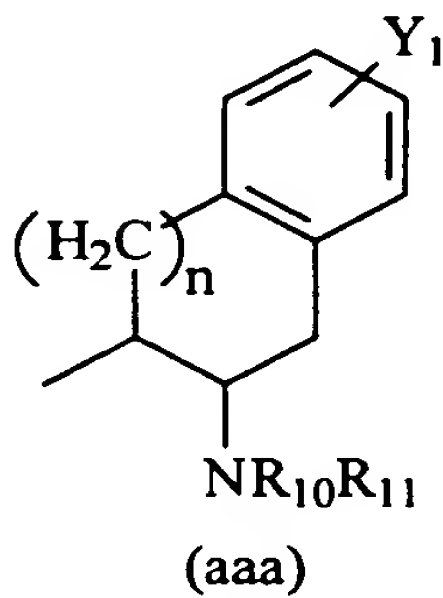
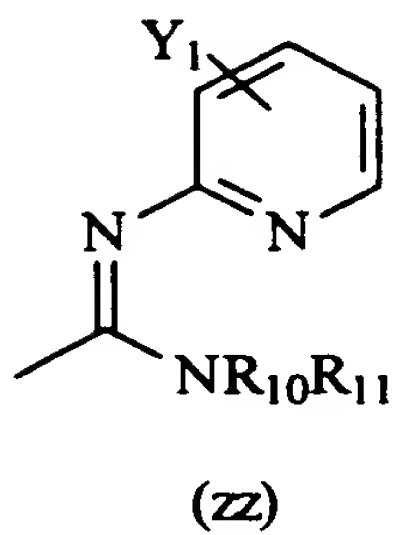
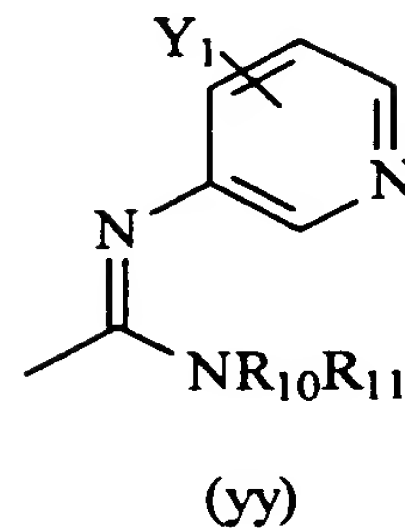
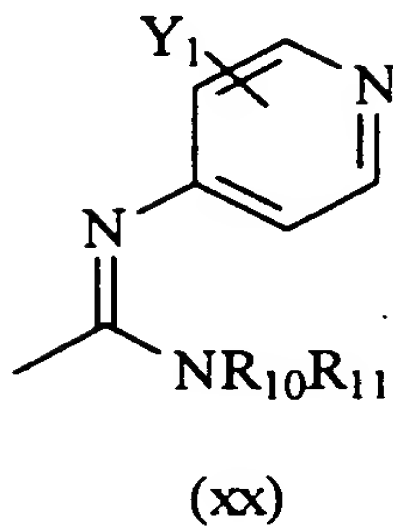
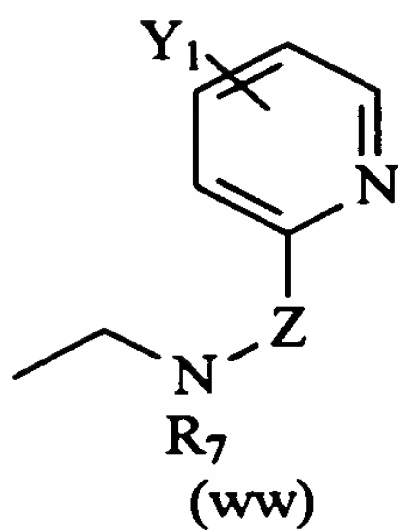
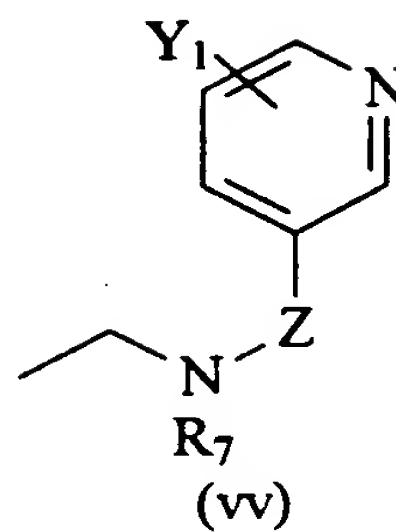
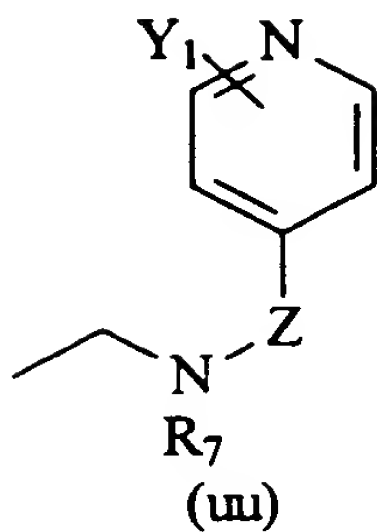
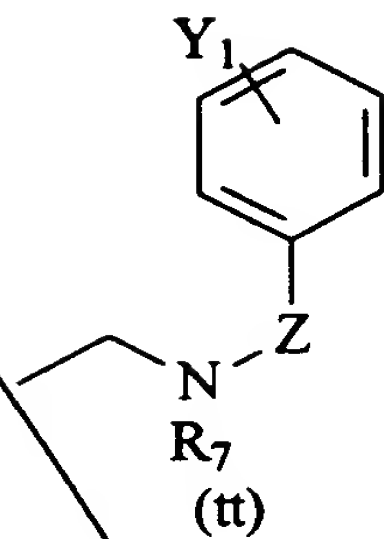


(aa)

Station	1955-1956	1956-1957	1957-1958	1958-1959	1959-1960	1960-1961	1961-1962	1962-1963	1963-1964	1964-1965	1965-1966	1966-1967	1967-1968	1968-1969	1969-1970	1970-1971	1971-1972	1972-1973	1973-1974	1974-1975	1975-1976	1976-1977	1977-1978	1978-1979	1979-1980	1980-1981	1981-1982	1982-1983	1983-1984	1984-1985	1985-1986	1986-1987	1987-1988	1988-1989	1989-1990	1990-1991	1991-1992	1992-1993	1993-1994	1994-1995	1995-1996	1996-1997	1997-1998	1998-1999	1999-2000	2000-2001	2001-2002	2002-2003	2003-2004	2004-2005	2005-2006	2006-2007	2007-2008	2008-2009	2009-2010	2010-2011	2011-2012	2012-2013	2013-2014	2014-2015	2015-2016	2016-2017	2017-2018	2018-2019	2019-2020	2020-2021	2021-2022	2022-2023	2023-2024	2024-2025	2025-2026	2026-2027	2027-2028	2028-2029	2029-2030	2030-2031	2031-2032	2032-2033	2033-2034	2034-2035	2035-2036	2036-2037	2037-2038	2038-2039	2039-2040	2040-2041	2041-2042	2042-2043	2043-2044	2044-2045	2045-2046	2046-2047	2047-2048	2048-2049	2049-2050	2050-2051	2051-2052	2052-2053	2053-2054	2054-2055	2055-2056	2056-2057	2057-2058	2058-2059	2059-2060	2060-2061	2061-2062	2062-2063	2063-2064	2064-2065	2065-2066	2066-2067	2067-2068	2068-2069	2069-2070	2070-2071	2071-2072	2072-2073	2073-2074	2074-2075	2075-2076	2076-2077	2077-2078	2078-2079	2079-2080	2080-2081	2081-2082	2082-2083	2083-2084	2084-2085	2085-2086	2086-2087	2087-2088	2088-2089	2089-2090	2090-2091	2091-2092	2092-2093	2093-2094	2094-2095	2095-2096	2096-2097	2097-2098	2098-2099	2099-2100	2100-2101	2101-2102	2102-2103	2103-2104	2104-2105	2105-2106	2106-2107	2107-2108	2108-2109	2109-2110	2110-2111	2111-2112	2112-2113	2113-2114	2114-2115	2115-2116	2116-2117	2117-2118	2118-2119	2119-2120	2120-2121	2121-2122	2122-2123	2123-2124	2124-2125	2125-2126	2126-2127	2127-2128	2128-2129	2129-2130	2130-2131	2131-2132	2132-2133	2133-2134	2134-2135	2135-2136	2136-2137	2137-2138	2138-2139	2139-2140	2140-2141	2141-2142	2142-2143	2143-2144	2144-2145	2145-2146	2146-2147	2147-2148	2148-2149	2149-2150	2150-2151	2151-2152	2152-2153	2153-2154	2154-2155	2155-2156	2156-2157	2157-2158	2158-2159	2159-2160	2160-2161	2161-2162	2162-2163	2163-2164	2164-2165	2165-2166	2166-2167	2167-2168	2168-2169	2169-2170	2170-2171	2171-2172	2172-2173	2173-2174	2174-2175	2175-2176	2176-2177	2177-2178	2178-2179	2179-2180	2180-2181	2181-2182	2182-2183	2183-2184	2184-2185	2185-2186	2186-2187	2187-2188	2188-2189	2189-2190	2190-2191	2191-2192	2192-2193	2193-2194	2194-2195	2195-2196	2196-2197	2197-2198	2198-2199	2199-2200	2200-2201	2201-2202	2202-2203	2203-2204	2204-2205	2205-2206	2206-2207	2207-2208	2208-2209	2209-2210	2210-2211	2211-2212	2212-2213	2213-2214	2214-2215	2215-2216	2216-2217	2217-2218	2218-2219	2219-2220	2220-2221	2221-2222	2222-2223	2223-2224	2224-2225	2225-2226	2226-2227</
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[illegible]

[illegible]

X_1 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl;

X_2 is hydrogen, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl;

or X_1 and X_2 together form $=O$, $=S$, $=NH$;

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $NR_{10}R_{11}$,

5 $NHCO R_{12}$, $NHCO_2 R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_n Y_2$, $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CONR_{13}R_{14}$,
 $CH_2(CH_2)_n Y_2$;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$;

and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 , $CH_2(CH_2)_n Y_2$
and pharmaceutically acceptable salts thereof.

8. The kappa opioid receptor antagonist compound of claim 7, wherein R_1 , R_4 , R_5 , Y_1 ,
20 Y_2 , Z , n , X_1 , X_2 , and R_7 - R_{17} are as indicated above;

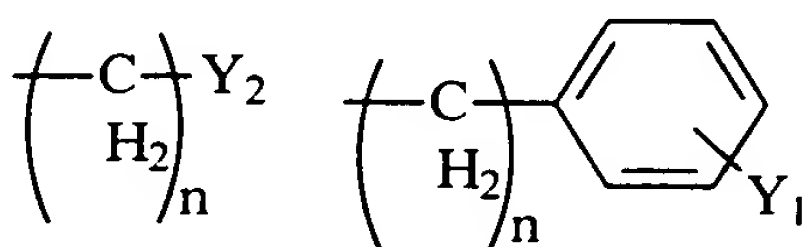
Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, CH_2 aryl
substituted by one or more substituents Y_1 ; and

R_6 is a group having a formula selected from the group consisting of structures (a)-
25 (cc).

9. The kappa opioid receptor antagonist compound of claim 7, wherein Y_1 , Y_2 , R_4 , R_5 ,
 Z , n , X_1 , X_2 and R_8 - R_{15} are as indicated above;

R_1 is C_{1-8} alkyl,



Y₃ is H;

R₂ and R₃ are each, independently, H or C₁₋₈ alkyl, wherein R₂ and R₃ cannot both be H at the same time;

R₆ is a formula selected from the structures (a)-(r) shown above; and

R₇ is H, C₁₋₈ alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

10. The kappa opioid receptor antagonist compound of claim 7, wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₅ are as noted above;

R₁ is C₁₋₈ alkyl;

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, COCH₂R₉;

Y₃ is H;

R₂ and R₃ are each, independently, H or methyl, wherein R₂ and R₃ cannot both be H at the same time;

R₄ is H, C₁₋₈ alkyl, CO₂C₁₋₈alkyl, aryl substituted by one or more substituents Y₁ and the stereocenter adjacent to R₄ is in an (S) configuration;

R₅ is H, C₁₋₈ alkyl, CH₂CO₂C₁₋₈ alkyl;

R₆ is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

11. The kappa opioid receptor antagonist compound of claim 7, wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₄ are as indicated above;

R₁ is methyl,

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, COCH₂R₉;

Y₃ is H;

R₂ and R₃ are each H or methyl, such that when R₂ is H, R₃ is methyl and vice versa;

R_4 is C_{1-8} alkyl, CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

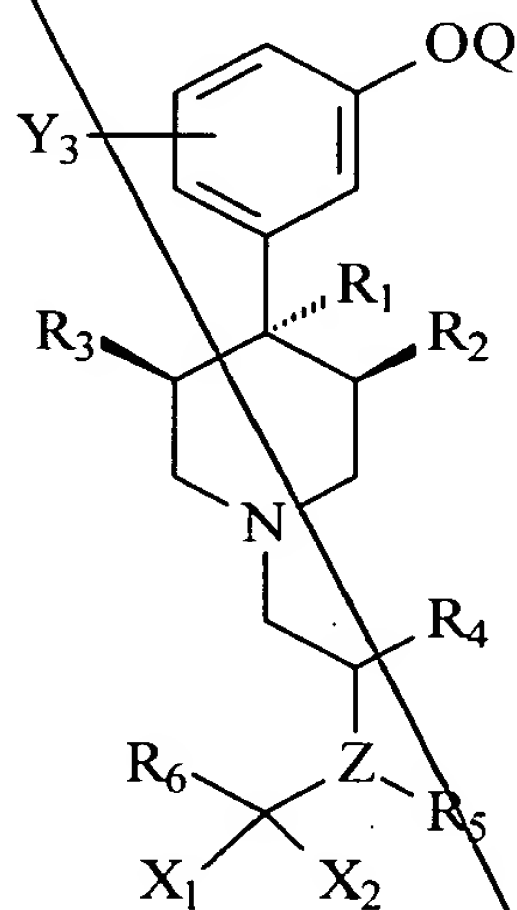
R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

12. The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae 14-21 of Fig. 1.

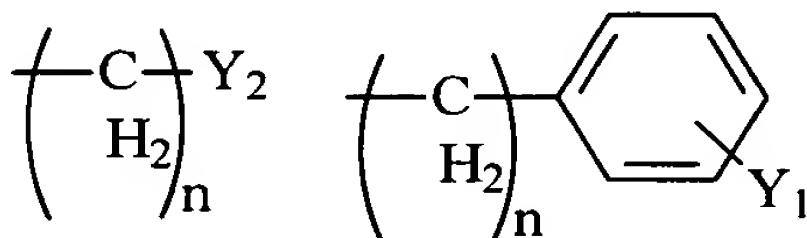
13. A pharmaceutical composition comprising:
an effective amount of a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):

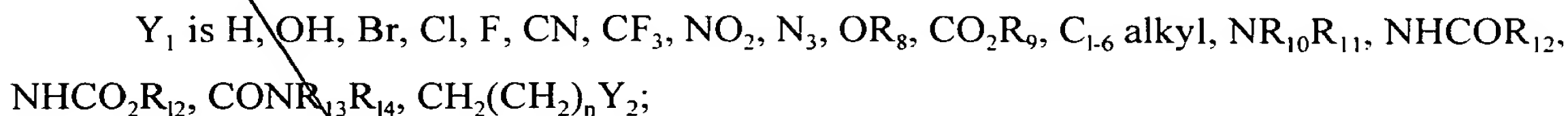


(I)

wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:





Y_3 is H, OH, Br, Cl, F, CN, CF_3 , NO_2 , N_3 , OR_8 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, $CH_2(CH_2)_nY_2$;

~~R₃ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl or CH₂aryl substituted by one or more groups Y₁.~~

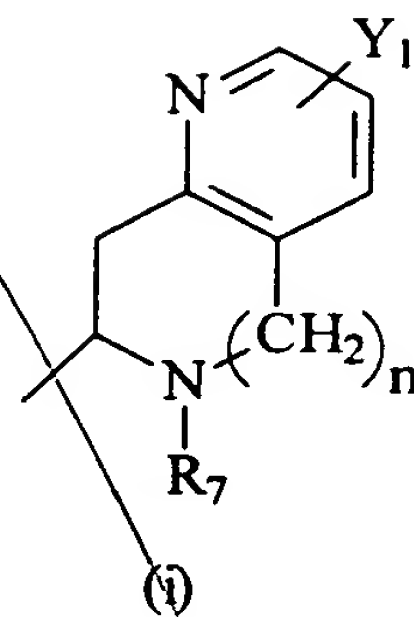
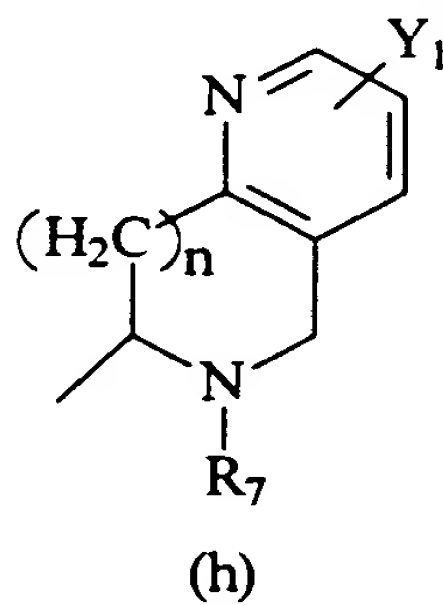
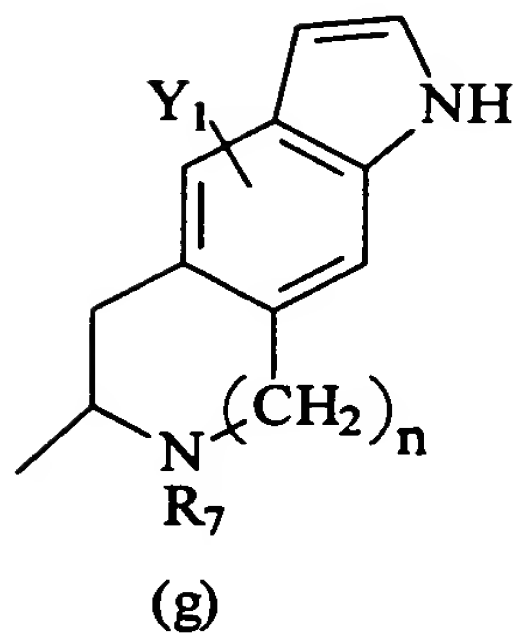
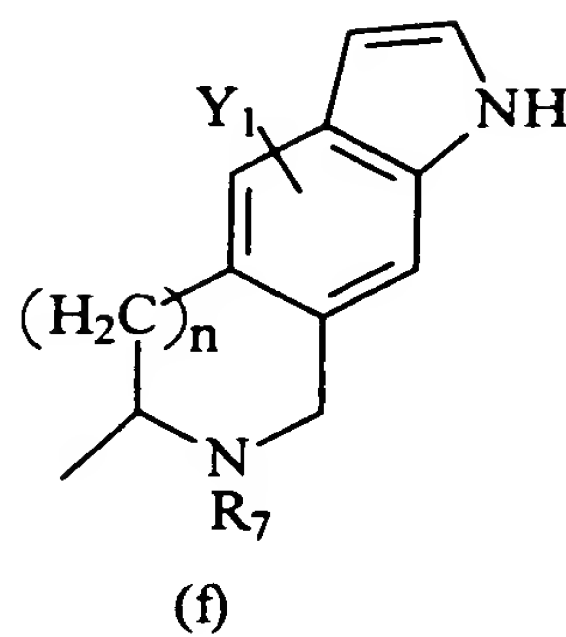
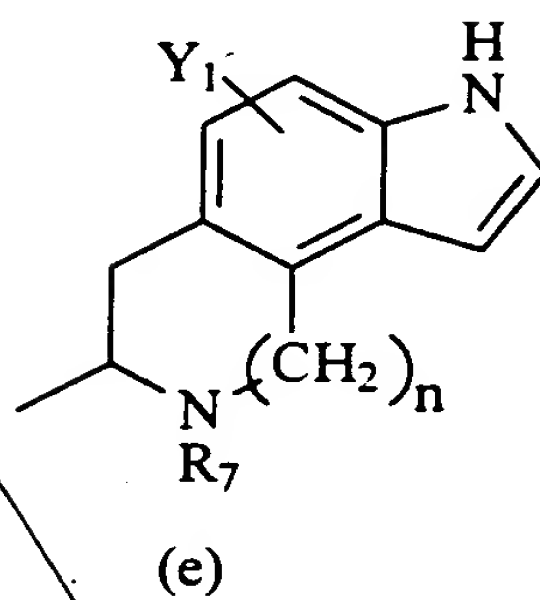
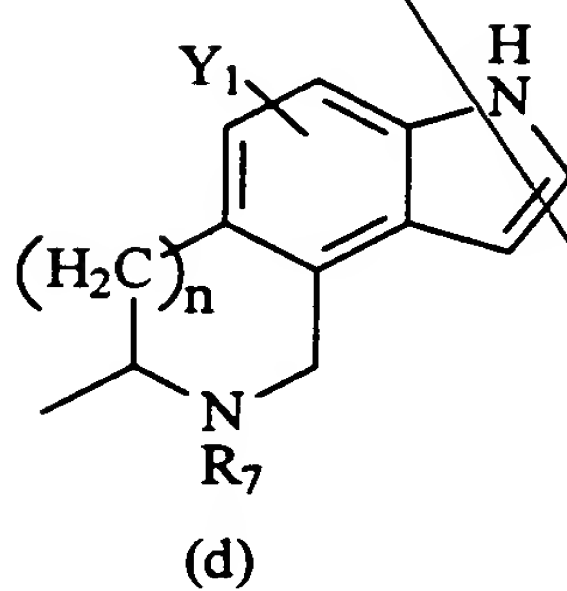
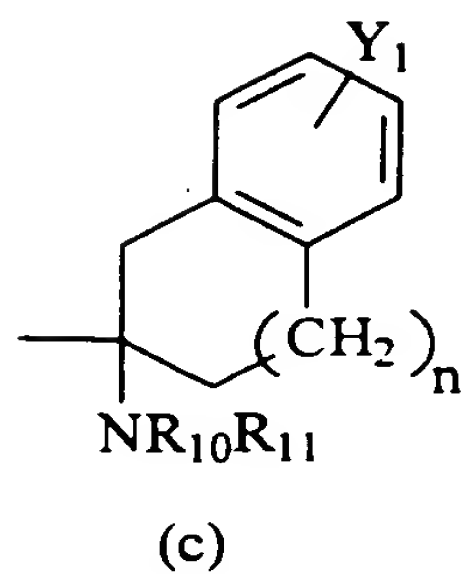
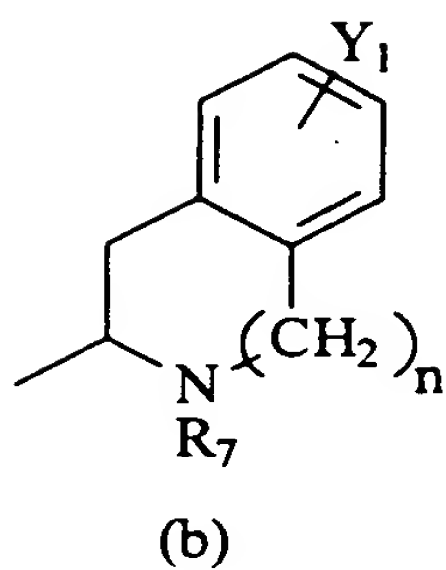
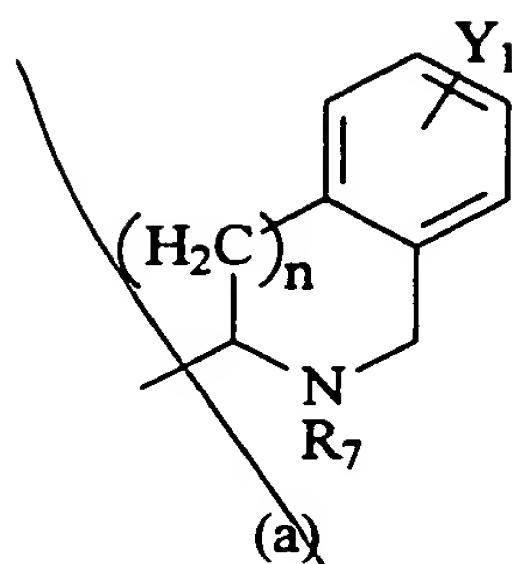
~~R₄ is hydrogen, C₁₋₈ alkyl, CO₂C₁₋₈ alkylaryl substituted by one or more groups Y₁, CH₂aryl substituted by one or more groups Y₁, or CO₂C₁₋₈ alkyl;~~

R₅ is H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, CH₂CO₂C₁₋₈ alkyl, CO₂C₁₋₈ alkyl or CH₂aryl substituted by one or more groups Y₁;

R_6 is a group selected from the group consisting of structures (a)-(bbb):

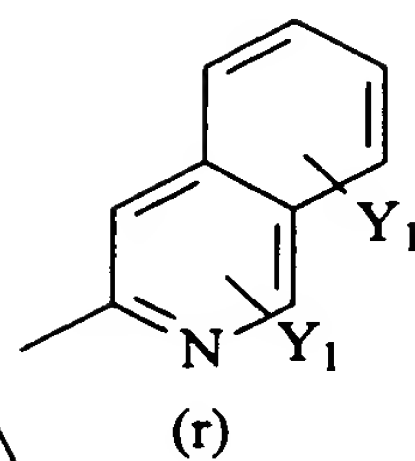
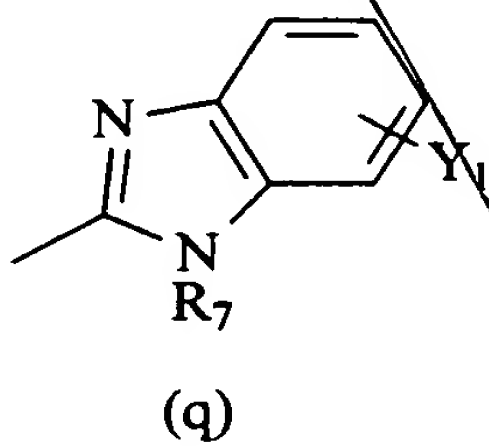
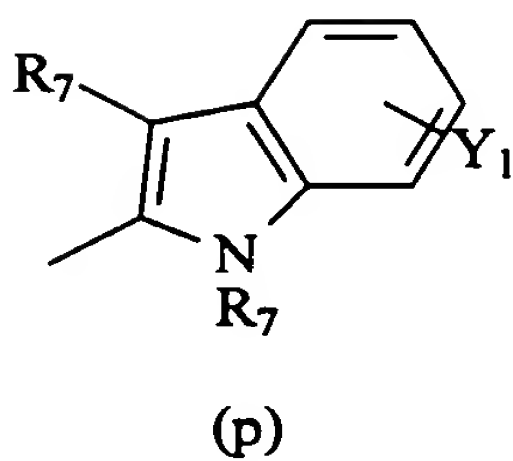
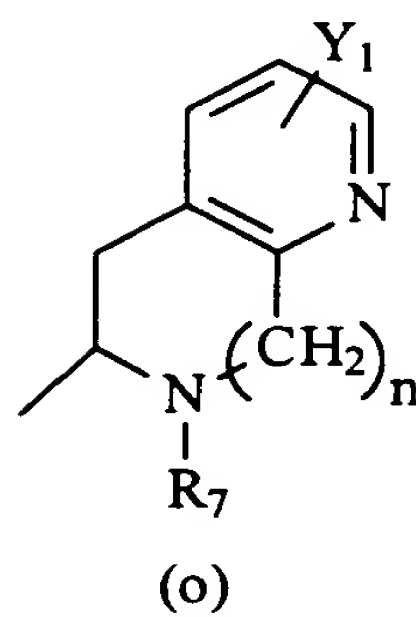
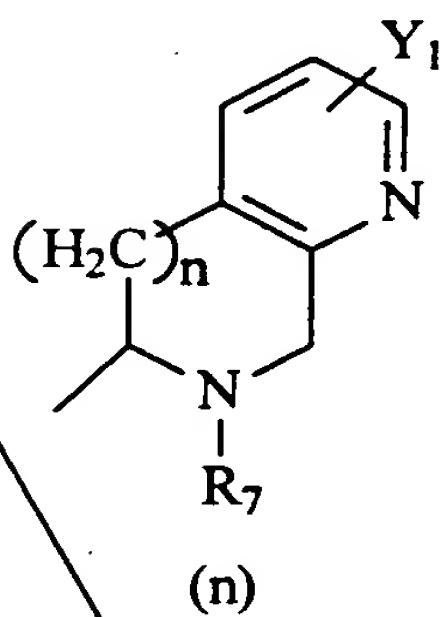
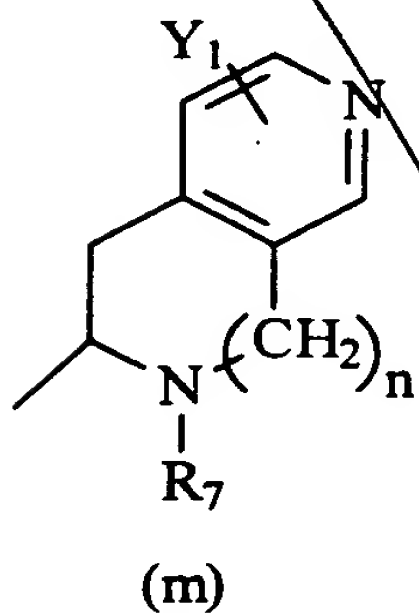
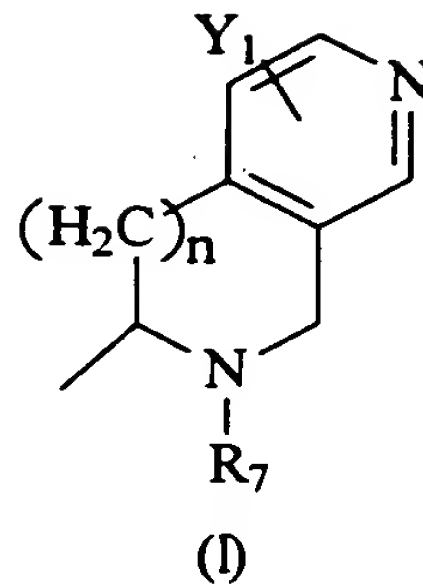
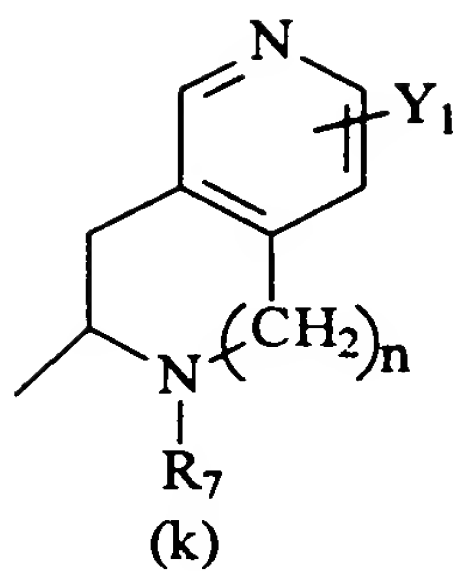
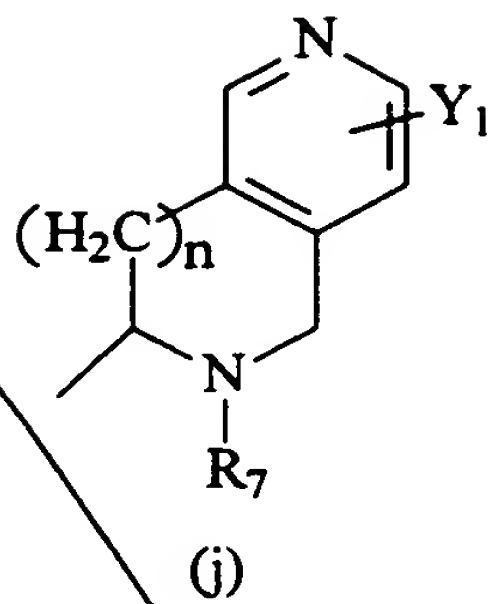
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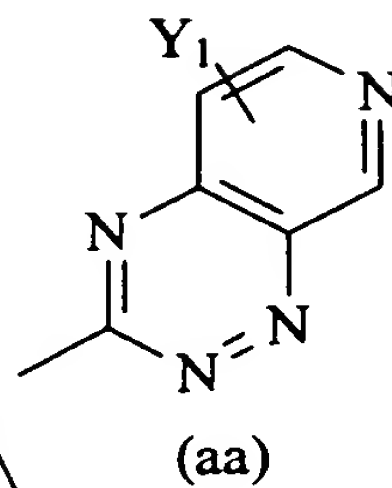
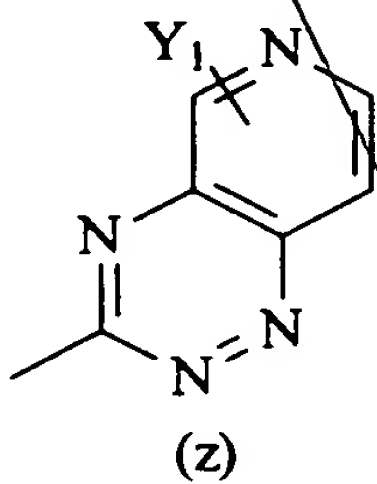
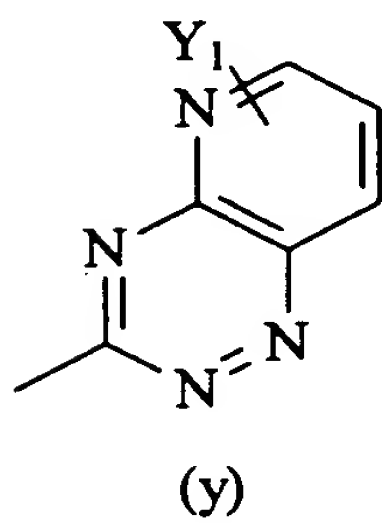
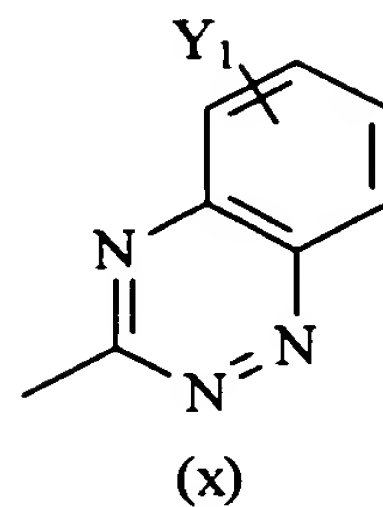
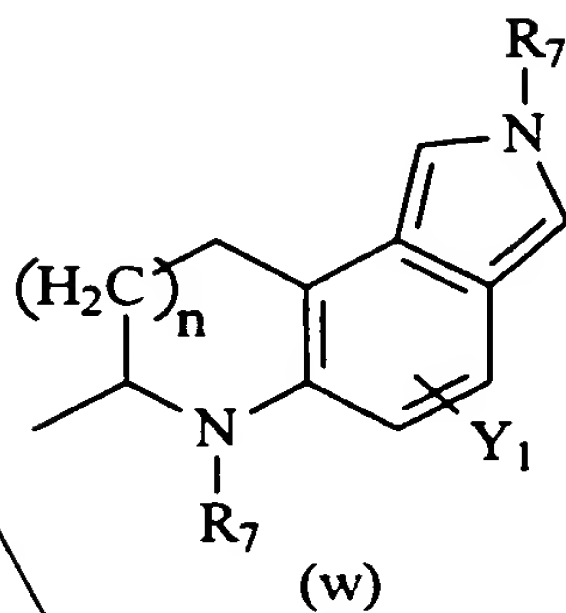
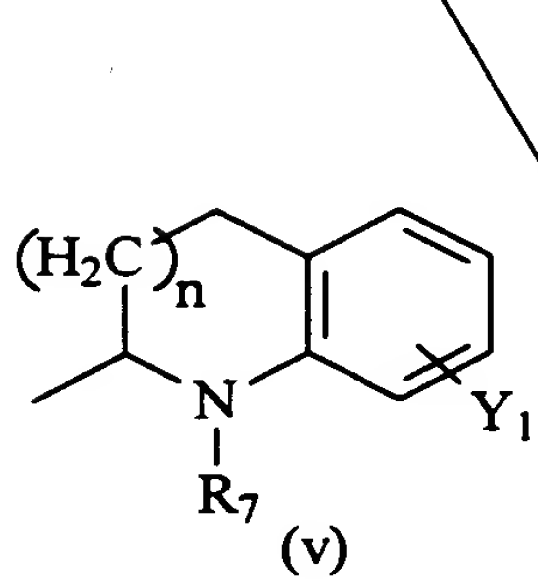
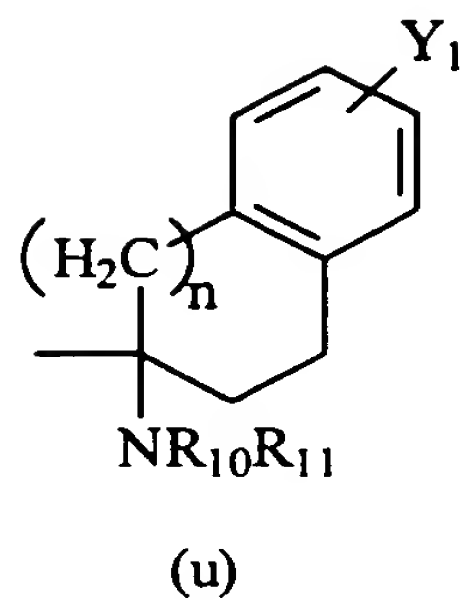
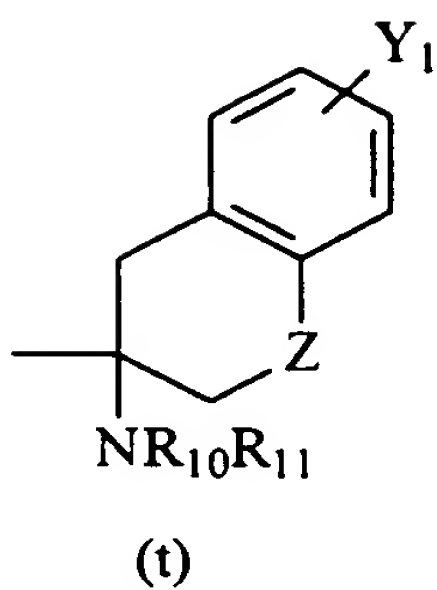
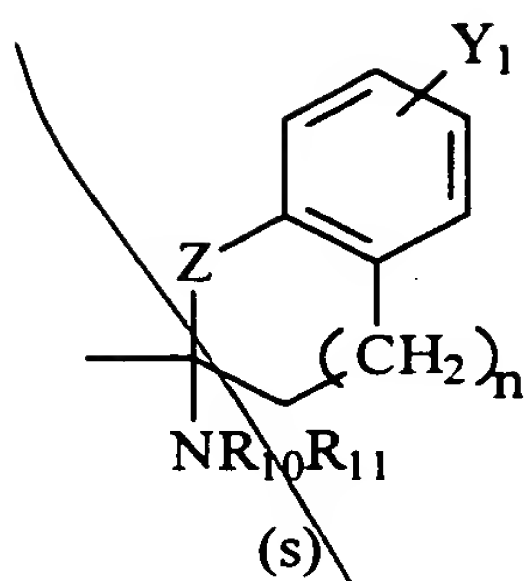
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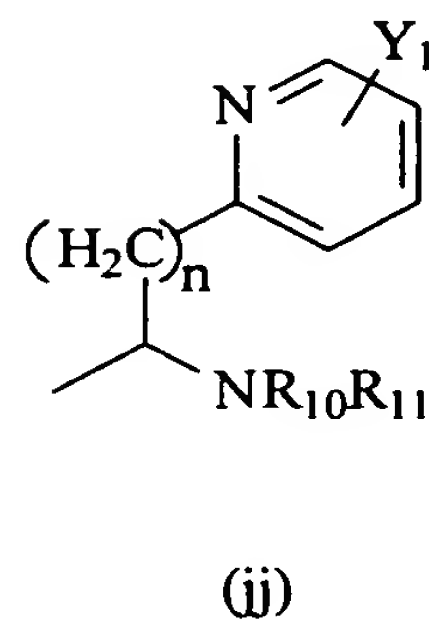
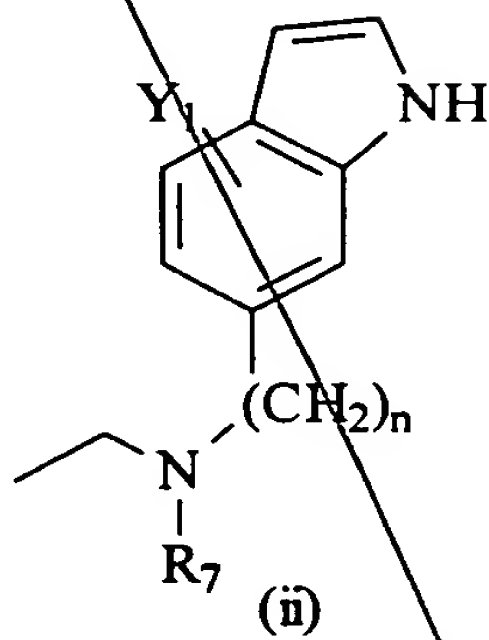
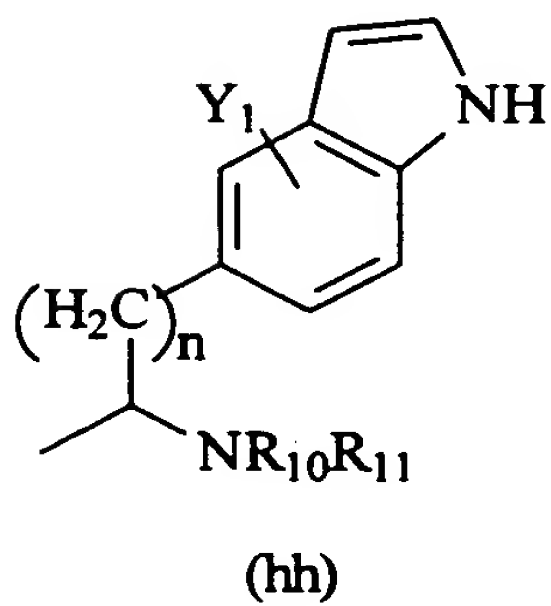
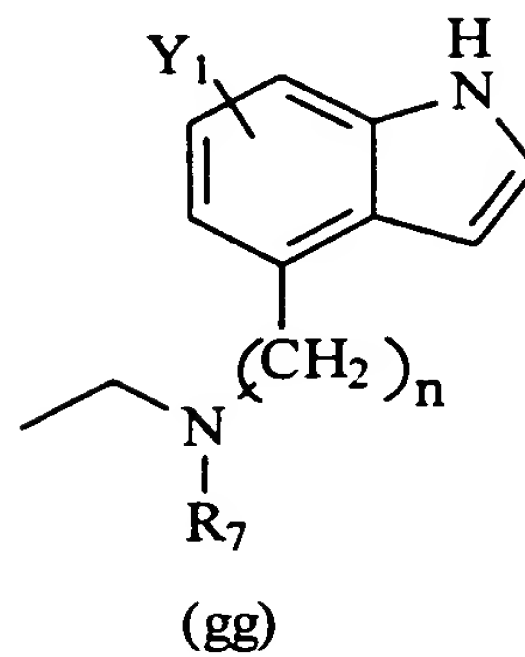
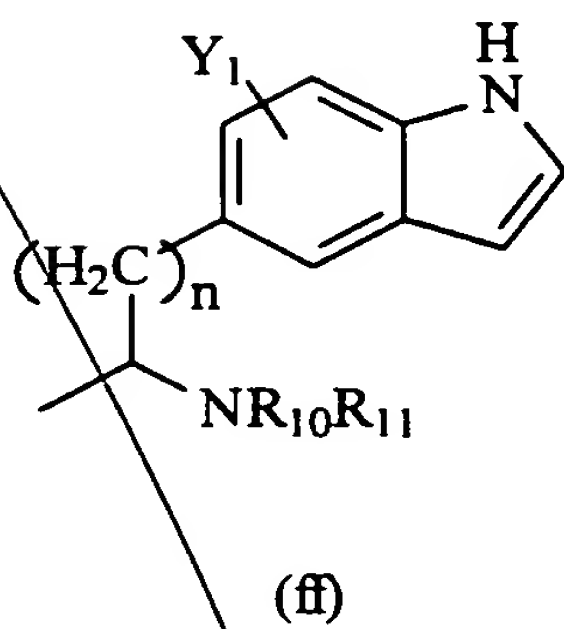
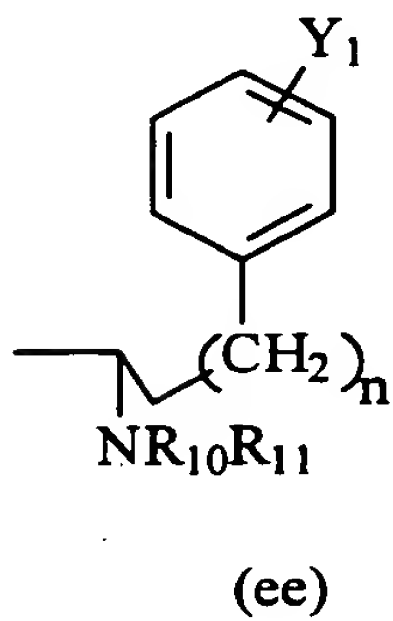
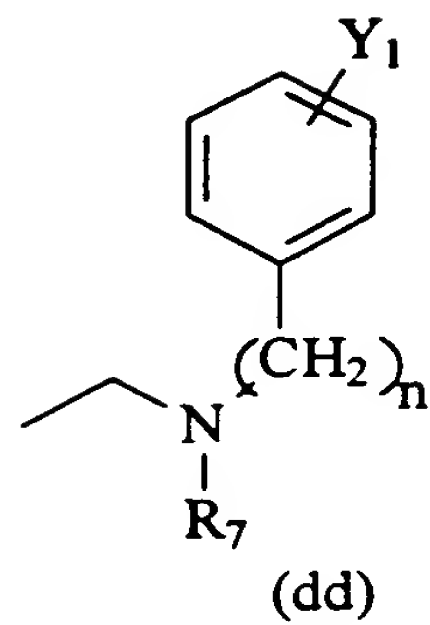
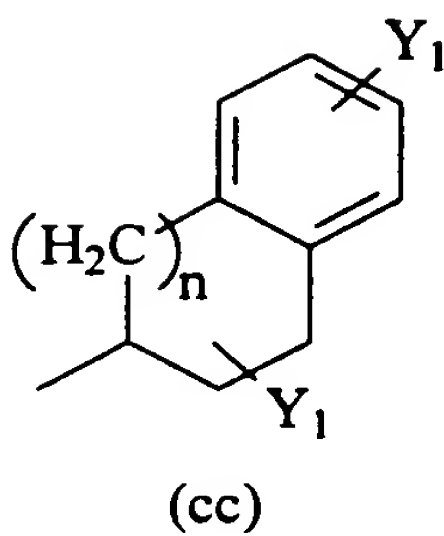
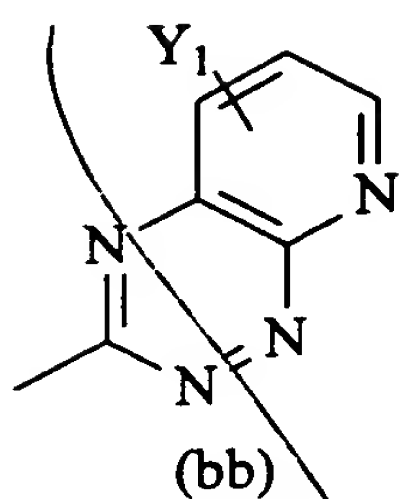
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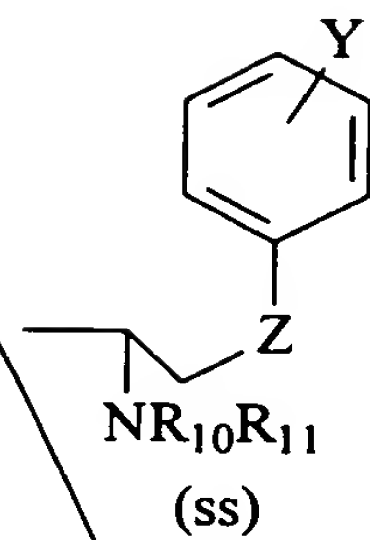
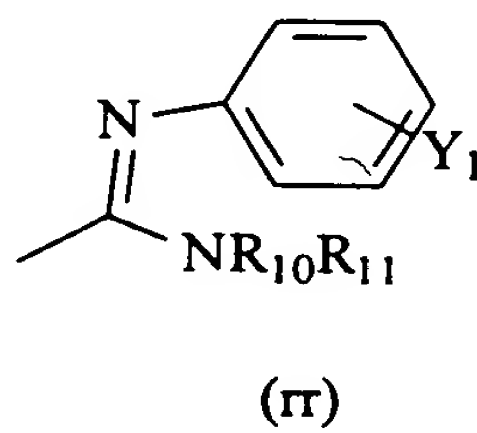
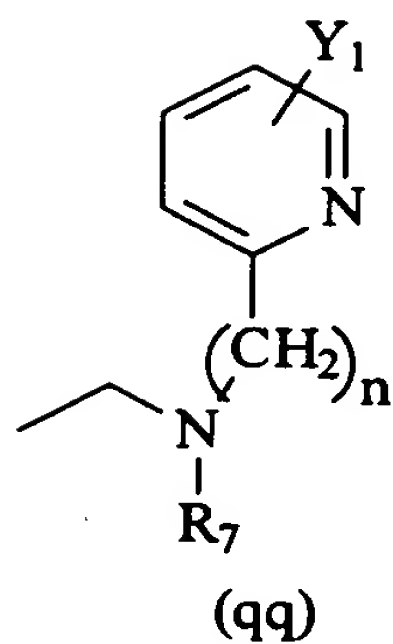
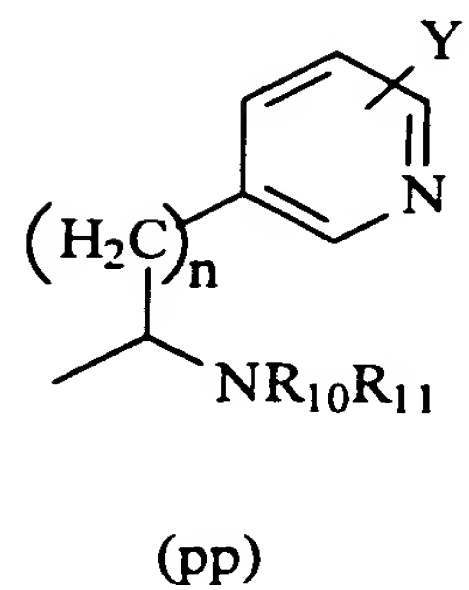
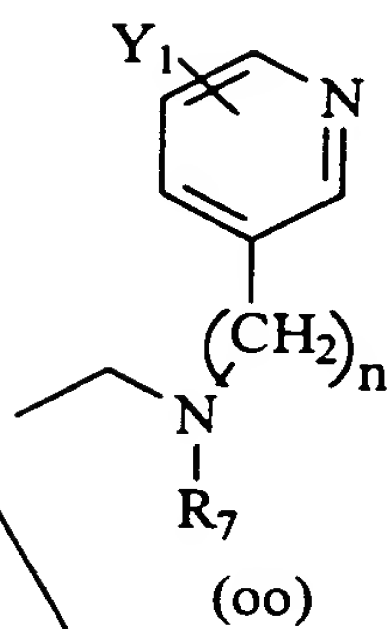
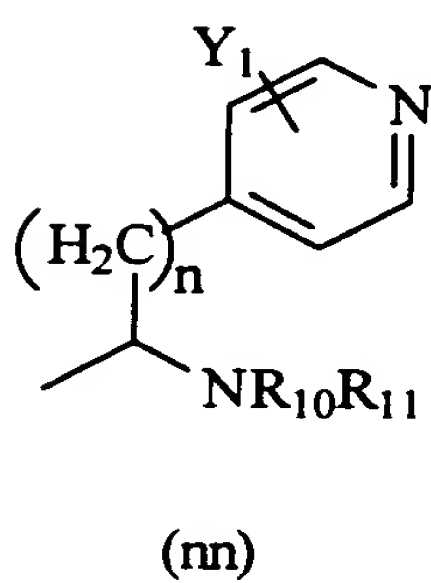
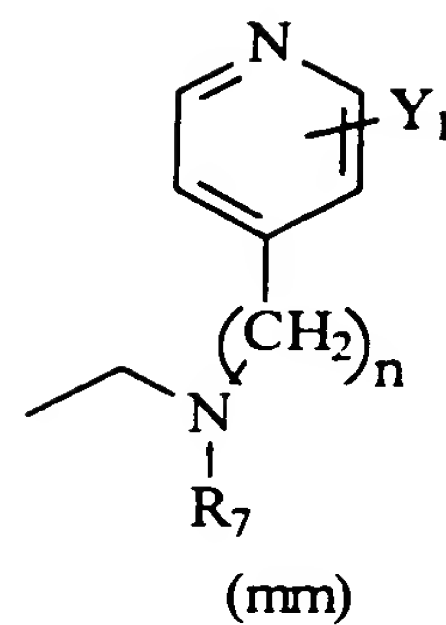
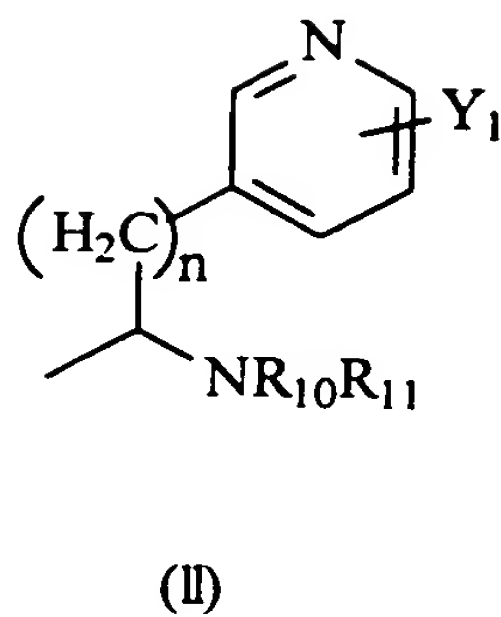
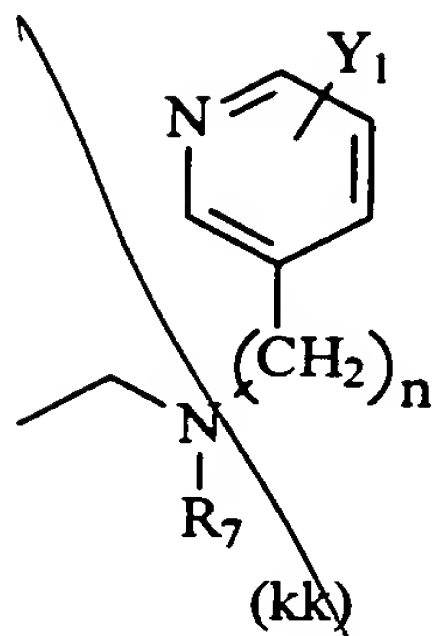
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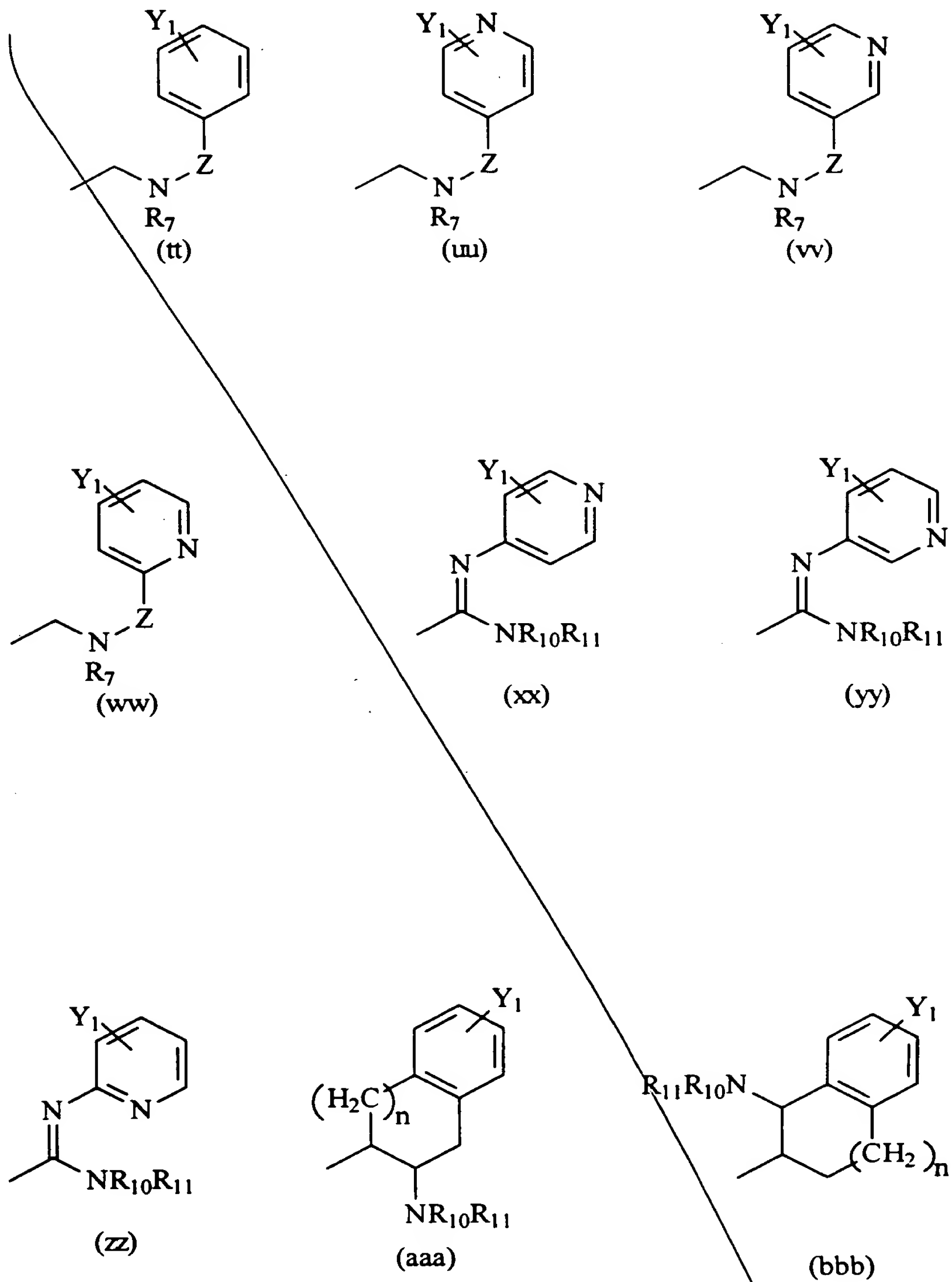
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X₁ is hydrogen, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl;

X₂ is hydrogen, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl;

or X₁ and X₂ together form =O, =S, =NH;

R₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, NR₁₀R₁₁,

5 NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, CH₂(CH₂)_nY₂, C(=NH)NR₁₆R₁₇.

R₈ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CONR₁₃R₁₄,
CH₂(CH₂)_nY₂;

R₉ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₀ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₁ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₂ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₃ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₄ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₅ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

R₁₆ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂;

and

R₁₇ is H, C₁₋₈ alkyl, CH₂ aryl substituted by one or more substituents Y₁, CH₂(CH₂)_nY₂
or a pharmaceutically acceptable salt thereof.

14. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor
antagonist is a compound of formula (I), wherein R₁, R₄, R₅, Y₁, Y₂, Z, n, X₁, X₂, and R₇-R₁₇
are as indicated above;

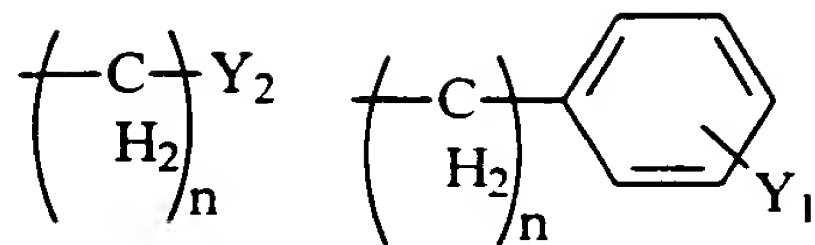
Y₃ is H;

R₂ and R₃ are each, independently, H, C₁₋₈ alkyl, C₃₋₈ alkenyl, C₃₋₈ alkynyl, CH₂ aryl
substituted by one or more substituents Y₁; and

25 R₆ is a group having a formula selected from the group consisting of structures (a)-
(cc).

15. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor
antagonist is a compound of formula (I), wherein Y₁, Y₂, R₄, R₅, Z, n, X₁, X₂ and R₈-R₁₅ are as
indicated above;

30 R₁ is C₁₋₈ alkyl,



Y₃ is H;

R₂ and R₃ are each, independently, H or C₁₋₈ alkyl, wherein R₂ and R₃ cannot both be H at the same time;

R₆ is a formula selected from the structures (a)-(r) shown above; and

R₇ is H, C₁₋₈ alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

16. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y₁, Z, n, X₁, X₂ and R₈-R₁₅ are as noted above;

R₁ is C₁₋₈ alkyl;

Y₂ is H, CF₃, CO₂R₉, C₁₋₆ alkyl, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₂, CONR₁₃R₁₄, CH₂OH, CH₂OR₈, COCH₂R₉;

Y₃ is H;

R₂ and R₃ are each, independently, H or methyl, wherein R₂ and R₃ cannot both be H at the same time;

R₄ is H, C₁₋₈ alkyl, CO₂C₁₋₈alkyl, aryl substituted by one or more substituents Y₁ and the stereocenter adjacent to R₄ is in an (S) configuration;

R₅ is H, C₁₋₈ alkyl, CH₂CO₂C₁₋₈ alkyl;

R₆ is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R₇ is H, C₁₋₈alkyl, CH₂aryl substituted by one or more substituents Y₁, NR₁₀R₁₁, NHCOR₁₂, NHCO₂R₁₃, CONR₁₄R₁₅, or CH₂(CH₂)_nY₂.

17. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1 , Z , n , X_1 , X_2 and R_8 - R_{14} are as indicated above;

R_1 is methyl,

Y_2 is H , CF_3 , CO_2R_9 , C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH , CH_2OR_8 , $COCH_2R_9$;

Y_3 is H ;

R_2 and R_3 are each H or methyl, such that when R_2 is H , R_3 is methyl and vice versa;

R_4 is C_{1-8} alkyl, CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R_5 is H ;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H , C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

18. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1.

19. The pharmaceutical composition of claim 13, wherein said composition is an injectable composition.

20. The pharmaceutical composition of claim 13, wherein said composition is an orally administrable composition.

21. The pharmaceutical composition of claim 20, wherein said orally administrable composition is in a form selected from the group consisting of tablets, capsules, troches, powders, solutions, dispersions, emulsions and suspensions.

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